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**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
18 SUBSTANCES**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

CONSULTATION ON 18 ONTARIO AIR STANDARDS

INFORMATION SUMMARY

Introduction

The Ministry is posting, for a 90-day public review, proposals for 18 air quality standards for which *Information Drafts* were posted on the Ministry's EBR Registry on 22nd January, 1999. These drafts provided stakeholders with the opportunity to submit additional information they felt should be considered by the Ministry in setting air quality standards for the respective substances. Based on the comments received and further internal review, the Ministry is now proposing Ambient Air Quality Criteria (AAQC) and Point of Impingement (POI) standards for the chemicals shown in Table I below. A detailed rationale document for each of the 18 air standards is available on the Environmental Bill of Rights Registry:

http://www.ene.gov.on.ca/envision/env_reg/er/registry.htm

Table I: 18 Proposed Air Standards

Chemical	Ambient Air Quality Criterion (24 hour)		Point of Impingement Standard/Guideline (half hour)		
	Current	Proposed	Current	Proposed Standard	Proposed Range for Interim Standard
<i>Acrylonitrile*</i>	100	0.6	300 (G)	1.8	1.8 to 180
<i>Ammonia</i>	3600	100	3600 (S)	300	300 to 3000
<i>Chlorine</i>	150	10	300 (S)	30	30 to 300
<i>Chloroform*</i>	500	1	1500 (G)	3	3 to 300
<i>Ethyl benzene</i>	4000 [†]	1000	4000 (S)	1400	Not Required
<i>Ethyl ether</i>	30000	8000	30000 (G)	700	700 to 7000
<i>n-Heptane</i>	none	11000	none	33000	Not Required
<i>n-Hexane</i>	12000	200	35000 (G)	600	600 to 6000
<i>Hydrogen chloride</i>	40	20	100 (S)	100	Not Required
<i>Isopropyl benzene</i>	100 [†]	400	100 (G)	100	Not Required
<i>Methanol</i>	28000	3100	84000 (S)	9300	Not Required
<i>Methyl ethyl ketone</i>	31000 [†]	1000	31000 (S)	3000	3000 to 30000
<i>Methyl isobutyl ketone</i>	1200	1200	1200 (G)	1200	Not Required
<i>Mineral spirits</i>	10000	2600	30000 (G)	3000	3000 to 30000
<i>Propylene oxide*</i>	4500	1.5	13500 (G)	4.5	4.5 to 450
<i>Toluene</i>	2000	2000	2000 (S)	2000	Not Required
<i>Vinylidene chloride</i>	35	10	70 (G)	30	Not Required
<i>Xylene</i>	2300	1500	2300 (S)	2300	Not Required

Notes: concentrations expressed in micrograms per cubic metre of air ($\mu\text{g}/\text{m}^3$)

* carcinogens

(S) standard

(G) guideline

† 1 hr guideline

Air Standards in Ontario

Ontario regulates air emissions in order to achieve and maintain air quality to ensure a healthy and safe environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated Point of Impingement standards and Point of Impingement guidelines in reviewing Certificates of Approval, each of which is derived by mathematical scaling, from an Ambient Air Quality Criterion. AAQCs represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of Impingement (POI) standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that at a source cannot, "cause or permit the concentration of a contaminant at a Point of Impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect. Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time the guidelines are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

- for carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;

- for non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to these postings. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

Objectives of this Consultation

The Ministry is committed to developing standards which are protective of human health and the environment and which can be implemented in a timely and equitable manner. Stakeholder consultation is critical to the success of the standard setting process to ensure that the full range of risk assessment and risk management issues, including economic considerations, are addressed during the development of standards.

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed

standard; including

- projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for the substances in Table I. In some cases, where it is not feasible to provide all of the information noted within the comment

period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), "*Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects*" Economic Services Branch- April 1994, and;
- "*Framework for the Application of Socio-economic Analyses in Setting Environmental Standards.*" Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Next Steps

- (1) The Ministry will review any comments received on these 18 proposed air quality standards and decide which standards can be finalized and which require risk management discussions. Decision notes on finalized standards will appear on the EBR. The Ministry will also initiate risk management discussions with affected stakeholders to further discuss the proposed final POI standard.
- (2) The Ministry's updated Standards Plan of November 1999 – *Setting Environmental Quality Standards in Ontario: The Ministry of the Environment's Standards Plan* – identified 70 high priority substances for air standards development. The next group of substances for which standards will be proposed are listed below. Currently, the Ministry is completing Information Drafts for these substances (except uranium which will be a proposal for a standard) and these will be posted on the EBR later this year.

Chemical Name

Chemical Abstract Services (CAS) Number

Acetone	(67-64-1)
Acetonitrile	(75-05-8)
Acrolein	(107-02-8)
Acrylamide	(79-06-1)

Cyclohexane	(110-82-7)
Di(2-ethylhexyl)phthalate	(117-81-7)
Di- <i>n</i> -octylphthalate	(117-84-0)
Hexamethylene diisocyanate monomer and biuret (HDI trimer)	(822-06-0) (4035-89-6)
Hydrogen cyanide	(74-90-8)
Hydrogen fluoride	(7664-39-3)
Methane diphenyl diisocyanate	(101-68-8)
Methyl isocyanate	(624-83-9)
Phenol	(108-95-2)
Toluene diisocyanate	(584-84-9)
Uranium	(7440-61-1)
Vinyl chloride	(75-01-4)

Following the completion of air standards development to date and the 16 chemicals listed above, the chemicals listed in Table II, below, will remain from the original list of 70 high priority chemicals for air standards development

Table II: Remaining high priority chemicals for air standards development.

Arsenic (and compounds)	Manganese (and compounds)
Benzene**	Mercury**
Benzo[a]pyrene	Methyl chloride
Butadiene, 1-3	Nickel (and compounds)
Butanol, n-	Nitrogen oxides (NOx)**
Butanol, iso-	Ozone**
Cadmium (and compounds)	Particulate Matter (PM)**
Chlorinated dibenzo- <i>p</i> -dioxins (CDDs and furans)**	Phosphoric acid (as phosphates)
Chlorine dioxide	Propanol, iso-
Chloroethane	Propylene
Chromium (hexavalent form)	Sulphur dioxide**
Copper	Sulphuric acid
Dichloroethane, 1,1-	Total reduced sulphur (TRS)**
Diethylhexyl phthalate (DEHP)	Trimethylbenzene, 1,2,4-
Diethyl phthalate (DOP)	Vanadium
Ethylene	Zinc
Ethylene oxide	
** Being Developed Through One of Two Federal/Provincial Partnerships: Canada Wide Standards under the Canadian Council of Ministers of the Environment (CCME/CWS) or a Federal Provincial Working Group under the Canadian Environmental Protection Act (CEPA/FPAC).	

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
ACRYLONITRILE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Acrylonitrile was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1985. A review of the scientific and technical information relevant to setting an ambient air quality standard for acrylonitrile has previously been provided to stakeholders for their comments. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for acrylonitrile.

Acrylonitrile is a colourless liquid with a faintly sweet and pungent odour. It is widely used as a chemical intermediate in a variety of industrial and commercial products and processes. Acrylonitrile does not occur naturally in the environment. It is produced industrially on a large scale and is emitted in large amounts in the form of vapours, and in aqueous effluents from facilities producing and using the chemical. Acrylonitrile is used as a raw material in the manufacturing of acrylic and modacrylic fibres, and in the production of plastics, and styrene-acrylonitrile, nitrile rubbers, nitrile barrier resins, adiponitrile, and acrylamide.

Acrylonitrile is not currently produced in Canada and is only used in the manufacturing of other products. According to occupational exposure and emission data, there appears to be greater exposure to humans and the environment from the use of acrylonitrile in end-user plants (3,000 to 20,000 $\mu\text{g}/\text{m}^3$) compared to production facilities (100 to 4,000 $\mu\text{g}/\text{m}^3$). Similarly, acrylonitrile levels around user plants are greater than around producing plants. The majority of acrylonitrile emitted is released into the air. According to the data reported in the National Pollutant Release Inventory (NPRI) of Environment Canada, one facility is responsible for nearly all releases in Ontario. The total reported atmospheric releases in Ontario for the years of 1993, 1994, 1995, 1996 and 1997, were 16.6, 17.6, 14.2, 8.9 and 5.2 tonnes, respectively. Acrylonitrile is not routinely monitored in Canada, however, ambient air monitoring results from the MOE Air Quality Study in Windsor indicates that acrylonitrile levels were below the detection limits which ranged from 0.21 to 0.64 $\mu\text{g}/\text{m}^3$.

Humans can be exposed to acrylonitrile through air, water and food. It is absorbed by the body through inhalation, oral, and to some extent dermal routes. The reported odour detection thresholds range from 8,000 to 50,000 $\mu\text{g}/\text{m}^3$. Exposure to acrylonitrile at concentrations of 7 to 45 $\mu\text{g}/\text{m}^3$ for 20 to 45 minutes leads to irritation of the mucous membranes, nausea, headaches and nervous irritability. Individuals also experience low grade anaemia, leukocytosis, kidney irritation and mild jaundice.

however, these effects subside when the exposure to acrylonitrile is terminated. Results have shown that children are more sensitive than adults.

Acrylonitrile is classified as a probable human carcinogen (class B1) by the United States Environmental Protection Agency (US EPA). This is based upon the observation of a statistically significant increase of lung cancer in humans and astrocytomas (cancer of non-neuron supportive cells) in the brain of rats. The International Agency for Research in Cancer (IARC) has classified acrylonitrile as a probable human carcinogen (group 2A) on the basis of sufficient evidence of carcinogenicity for animals, and limited evidence for humans.

Data from animal carcinogenicity studies indicated a significant dose-dependent increase in cancer incidence, and may provide support to the carcinogenicity in humans. Genetic toxicology studies showed acrylonitrile induced gene mutations in bacteria, yeast, and mammalian cells, sister chromatid exchange in mammalian cells, and cell transformation of three different cell types. On the basis of these results, acrylonitrile is considered a non-threshold carcinogen. The Toxicology Excellence for Risk Assessment (TERA) has recommended that the carcinogenicity of acrylonitrile in humans be reviewed based on more recent data. Under the CEPA (*Canadian Environmental Protection Act*), Environment Canada and Health Canada have recently completed a health and environmental assessment for acrylonitrile and consider that this compound is toxic and carcinogenic to humans.

The US EPA has established an inhalation cancer unit risk for lifetime exposure to acrylonitrile of 6.8×10^{-5} per ($\mu\text{g}/\text{m}^3$). That is, for a lifetime exposure to this chemical, at an ambient air concentration of $0.01 \mu\text{g}/\text{m}^3$, the probability of a cancer incidence is one in a million. Agencies, such as New Jersey, Massachusetts, Michigan and New York, have adopted the assessment and unit risk estimate from the US EPA to derive their long-term guidelines. California developed its own cancer unit risk estimate which resulted in a more conservative guideline. The WHO established its cancer unit risk estimate based on the same epidemiological study used by the US EPA but employed a different method of calculation which resulted in a unit risk of 2×10^{-5} per ($\mu\text{g}/\text{m}^3$). Environment Canada and Health Canada have derived a tumourigenic concentration at 5% increase in tumour incidence (TC_{05}) of $6 \text{ mg}/\text{m}^3$, based on data in female rats. In addition, several states have adopted the US EPA Chronic (non-cancer) Reference Concentration (RfC) of $2 \mu\text{g}/\text{m}^3$ as a benchmark for shorter averaging periods.

The current AAQC for acrylonitrile in Ontario is $100 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time. The half-hour POI guideline is $300 \mu\text{g}/\text{m}^3$. Both criteria were established based on the protection of human health. In revising the air quality standards for Ontario, the Ministry of the Environment is reviewing and considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental

Medicine and the Canadian Federal Government. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepts the scientific rationale and risk assessment employed by Environment Canada and Health Canada to develop their TC_{05} value of 6 mg/m^3 . The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and $0.12 \text{ } \mu\text{g/m}^3$, representing excess cancer risk of 1 in 100,000 and 1 in 1,000,000, respectively. The Ministry proposes to derive an annual AAQC based on the risk specific concentration of $0.12 \text{ } \mu\text{g/m}^3$.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for acrylonitrile:

- **an annual average AAQC of $0.12 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound; and,**
- **a 24-hour average AAQC of $0.6 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $1.8 \text{ } \mu\text{g/m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $300 \text{ } \mu\text{g/m}^3$ to this revised level of $1.8 \text{ } \mu\text{g/m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$1.8 \text{ } \mu\text{g/m}^3$ to $180 \text{ } \mu\text{g/m}^3$ (micrograms per cubic metre of air) for acrylonitrile; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Acrylonitrile was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing guideline in 1985. A review of scientific and technical information relevant to setting an ambient air quality standard for acrylonitrile had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for acrylonitrile.

2.0 General Information

2.1 Physical and Chemical Properties

Acrylonitrile is a volatile, flammable, colourless liquid with a faintly sweet, yet, pungent odour. The following list provides some of its properties:

CAS #	39447
RTECS #	AT5250000
UN #	UN1093
Conversion Factors	1 ppm = 2.17 mg/m ³ at 25 °C
Boiling Point	77.3 °C
Melting Point	-82 °C
Henry's Law Constant	8.8x10 ⁻⁵ atm·m ³ /mol
Flash Point	0 °C
Density	0.806 at 20 °C
Water Solubility	73,500 mg/L
Log K _{ow}	-0.07
Formula	C ₃ H ₃ N
Molecular Weight	53.1 g/mol
Vapour Density (air = 1)	1.9
Vapour Pressure	100 mmHg at 23 °C
Common Synonyms	acrylic acid nitrile, acrylon, carbacryl, cyanoethylene, 2-propenenitrile, vinyl cyanide

The odour detection threshold, as reported by the American Industrial Hygiene Association (AIHA) is 1.6 ppm (3400 µg/m³; this is also the geometric mean of air odour threshold). Similarly, the American Conference of Government Industrial Hygienists (ACGIH) states an odour threshold of 9,700 µg/m³. The Quebec Workplace Health and Safety Commission is in general agreement with the ACGIH, listing an odour detection limit at 8,000 µg/m³ (CSST, 1997). The odour detection threshold for acrylonitrile in air has been reported to be as high as 47,000 µg/m³ (Verschuere, 1983). The odour recognition thresholds have been reported to range from 3,700 to 50,000 µg/m³ (Cheminfo, 1996).

2.2 Uses

Acrylonitrile is widely used as a chemical intermediate in a variety of industrial and commercial products and processes. Acrylonitrile is used as a raw material in the manufacturing of acrylic and modacrylic fibres, and in the production of plastics and styrene-acrylonitrile, nitrile rubbers, nitrile barrier resins, adiponitrile, and acrylamide (ATSDR, 1990). It has been used as a fumigant for stored tobacco, flour milling and bakery food processing equipment; however, this practice has since ceased (IARC, 1979).

2.3 Sources and Levels

Acrylonitrile does not occur naturally in the environment (Howard, 1989). It is produced industrially on a large scale (WHO, 1986) and is emitted in large amounts. Emissions, which are generally in the form of vapours or aqueous effluents, are by-products of both the facilities that generate acrylonitrile, as well as those plants that use acrylonitrile in the production of other products. Acrylonitrile has been detected in cigarette smoke at levels of 1 to 2 mg per cigarette (IARC 1979; US EPA, 1983). It has also been detected in car exhaust, and may be released from polyacrylic fibers and plastics (Howard, 1989).

Since 1972, acrylonitrile has not been produced in Canada, however it is still imported (CEPA, 1999). All of the imported acrylonitrile comes from the U.S., and the amount has declined over the past two decades from 21,000 tonnes in 1976 to 7,600 tonnes in 1994 (CEPA, 1999). According to the National Pollutant Release Inventory (NPRI, 1993, 1994, 1995, 1996, 1997), on a national scale, on-site releases of acrylonitrile into the Canadian environment (air, water and soil) were 18.6, 19.5, 16.32, 10.84 and 5.19 tonnes, respectively. Almost all of these releases came from air emissions. The major source of releases was the organic chemical industries (97.4 %) (CEPA, 1999). For that same period, total reported releases to air for the province of Ontario were as follows: 1993 - 16.6 tonnes, 1994 - 17.6 tonnes, 1995 - 14.2 tonnes, 1996 - 8.9, and 1997 - 5.19 tonnes. One facility located in Sarnia, Ontario is responsible for most of these releases.

Acrylonitrile does not occur at measurable concentrations in the ambient air (US EPA, 1995). In general, the estimated level of human adult exposure to acrylonitrile via air from non-occupational exposure is below the detection limit. Acrylonitrile is not produced in Canada, however, in the US, acrylonitrile is produced industrially and is emitted in significant quantities from industrial sources. The estimated level of exposure to acrylonitrile of a population living within a 5 km radius of a chemical production factory or waste site is 2 to 12 $\mu\text{g}/\text{m}^3$ (ATSDR, 1990), while the level for those living near industrial plants that use acrylonitrile is 1 to 325 $\mu\text{g}/\text{m}^3$ (a). The estimated exposure to acrylonitrile of workers in an acrylonitrile factory is 100 to 4,000 $\mu\text{g}/\text{m}^3$ (ATSDR, 1990). In contrast, exposure to workers in an acrylic fibre plant is 3,000 to 20,000 $\mu\text{g}/\text{m}^3$ (US EPA, 1994a). In general, it appears that

acrylonitrile levels are higher around factories that use the raw acrylonitrile in the production of other products, rather than near those factories that produce acrylonitrile (US EPA, 1983).

Acrylonitrile is not part of routine ambient air monitoring programmes in Canada, and no ambient data could be obtained from federal sources (Dann, 1997). Atmospheric acrylonitrile concentrations, at various sites in and around Windsor, were monitored by the Ontario Ministry of the Environment and Energy in 1991 using real-time measurement methods (detection limit, approximately 0.21 to 0.64 $\mu\text{g}/\text{m}^3$). The results indicated that any acrylonitrile levels in the air were below the detection limits (MOEE, 1997).

The estimated ground level concentration (GLC) values for acrylonitrile were extracted from Ontario Ministry of the Environment's Certificates of Approval. From a sample of seven companies the median concentration was 0.17 $\mu\text{g}/\text{m}^3$, ranging from a minimum of 0.1 $\mu\text{g}/\text{m}^3$ to a maximum of 15 $\mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

Acrylonitrile has a half-life in natural aquatic systems, primarily due to evaporation, ranging from 1 to 6 days, and secondarily due to biodegradation ranging from 6 to 21 days. In air, it is degraded primarily by photo-oxidation with a half-life of 9 hours to 9 days, depending upon atmospheric conditions. In soil, acrylonitrile evaporates rapidly or leaches into groundwater.

Environment Canada has determined that acrylonitrile has a Photochemical Ozone Creation Potential (POCP) of 25 which is considered moderate with regard to potential ozone formation (CEPA, 1999). However, actual contribution of photochemical ozone is dependent upon both reactivity and concentration of a substance. As acrylonitrile is only released from a few point sources within Canada and levels of acrylonitrile in ambient air within urban centres are generally below the detection limit of 0.9 $\mu\text{g}/\text{m}^3$, Environment Canada indicates that acrylonitrile causes only a very minor contribution to photochemical ozone formation (CEPA, 1999). Acrylonitrile is not expected to contribute to stratospheric ozone depletion and climate change (CEPA, 1999).

3.0 Toxicology of Acrylonitrile

The following toxicological review of acrylonitrile primarily focusses on the inhalation route of exposure, as this is the predominant pathway of human exposure, and since most of the released acrylonitrile is emitted to air. However, humans can also be exposed to acrylonitrile through, water and food, and it can enter the body by ingestion and to some extent via the dermal route (US EPA, 1983). Data on other exposure media are included in this document where relevant, or where inhalation data is lacking.

Acrylonitrile is absorbed rapidly after inhalation exposure. Within a few hours, approximately 40 - 50 % (exposed at 8.9 - 20 mg/m³) and 60 - 80% (exposed at 11 - 220 mg/m³) of the exposed concentrations have been found in the bodies of humans and animals, respectively (TERA, 1997). Absorption through the oral route is in the range of 90 - 98 % (TERA, 1997). Once absorbed, distribution through the body is rapid, with little potential for significant accumulation in any particular organ.

Acrylonitrile is metabolized by two major pathways which include, direct conjugation with glutathione, and oxidation by cytochrome P450 to 2-cyanoethylene oxide(CEO). 2-Cyanoethylene oxide is a mutagenic agent and alkylates DNA much more favourably than acrylonitrile (TERA, 1997; Woutersen, 1998). The CEO can be metabolized to cyanide, which may account for the acute toxicity of acrylonitrile. Acrylonitrile is detoxified through direct glutathione conjugation with acrylonitrile or with CEO. Species specificity in acrylonitrile metabolism has been reported between rats, mice and humans. More CEO is produced in mice than in rats and more CEO is metabolized to cyanide in mice. The kinetic parameters for rat and human microsomes were similar, and thus it was suggested that rats may be a good model species for the disposition of acrylonitrile for humans (TERA, 1997).

3.1 Acute Toxicity

Acute inhalation exposure to acrylonitrile may result in central nervous system effects such as headache, vertigo, nausea and convulsion (WHO, 1983; TERA, 1997). When humans are exposed to acrylonitrile concentrations of 7 to 45 µg/m³ for 20 to 45 minutes, they experience irritation of the mucous membranes, nausea, headaches and nervous irritability. (Wilson *et al*, 1948). Evidence suggests that acrylonitrile exposure may also induce alcohol intolerance and fatigue (Kaneko and Omae, 1992). Individuals also experience low grade anaemia, leukocytosis, kidney irritation and mild jaundice. These effects, however, subside when exposure to acrylonitrile stops (Wilson, 1944; Wilson *et al*, 1948). As is often the case, children are more sensitive to substances such as acrylonitrile than adults. In several instances, a child has died from inhalation of acrylonitrile vapour, whereas adults exposed to the same conditions experienced only minor irritations (ATSDR, 1990). The US Department of Health and Human Services calculated an acute (14-day) inhalation minimum risk level (MRL) of 1.5 ppm (3.15 mg/m³), based on a study (Jakubowski *et al*. 1987, as cited in ATSDR, 1990) showing neurological effects in workers.

In animals, observed LC₅₀ range from 300 - 990 mg/m³. Acute toxicity resembles cyanide poisoning which includes respiratory irritation and dysfunctioning of the central nervous system . (WHO, 1983; CEPA, 1999). Neurotoxicity following acute exposure develops in two phases. The first phase occurs shortly after exposure, likely due to the action of acrylonitrile, and resembles cholinergic over-stimulation, with effects such as vasodilation, extensive secretions such as the salivation, lacrimation, diarrhea and gastric secretion. The second phase is delayed by a few hours, likely caused by cyanide

toxicity, and manifested by central nervous disturbances such as trembling, ataxia, convulsions respiratory failure (TERA, 1997)

3.2 Subchronic and Chronic Toxicity

Chronic exposure can result in necrosis of the adrenal gland and the gastrointestinal tract, liver, kidney, lung and brain effects, dysfunctioning of the central nervous system and congestive lung oedema (TERA, 1997). A two-year study by Quast *et al.* (1980a, as cited in ATSDR, 1990) reported neurological effects (focal gliosis) and irritation of the nasal passage in rats exposed to 80 ppm (174 mg/m³). At this level of exposure no effects were noted in blood, liver or kidney.

Rats exposed to 10 mg/m³ acrylonitrile over 16 weeks had depressed T helper lymphocytes and T suppressor lymphocytes functions and diminished B lymphocyte transformation (Krivova *et al.*, 1982 as cited in WHO, 1983).

3.3 Developmental and Reproductive Toxicity

Murray *et al.* (1978, as cited in ATSDR, 1990 & WHO, 1983) exposed SD rats to 88,000 and 176,000 µg/m³ acrylonitrile vapour during the gestational period (6 to 15 days). The high dose group demonstrated a significant increase in foetal malformations. However, maternal toxicity was observed at both dose levels. Acrylonitrile teratogenicity was also demonstrated in hamsters resulting from intraperitoneal exposure on day 8 of gestation, with resulting malformations in the offspring (Willhite *et al.*, 1981 as cited in WHO, 1983).

Beliles *et al.* (1980 as cited in ATSDR, 1990) conducted a three-generation reproductive study on Charles River rats, administering acrylonitrile in drinking water. The results showed a reduction in both viability and lactation indices in the offspring as a result of maternal toxicity. Another study (Tandon *et al.*, 1988 as cited in ATSDR, 1990) suggests effects on male reproductive systems at 10 mg/kg/day.

3.4 Genotoxicity

Genotoxic properties of acrylonitrile are well documented and results have been mixed. In *in vitro* studies, acrylonitrile has elicited point mutations, clastogenic events, and has shown the ability to transform cells. Positive mutagenic responses have been observed in many genetic toxicology assays and on several phylogenetic levels from bacteria to humans.

Mutagenic activity was shown in prokaryotes (*Salmonella typhimurium* and *Escherichia coli*) and lower eukaryotes (*Saccharomyces cerevisiae*). A metabolic enzyme mixture was needed to elicit a mutagenic response with any strain of *Salmonella*, while *Escherichia coli* and *Saccharomyces*

cerevisiae produced positive results both in the presence or absence of metabolic enzymes (WHO, 1983). Gene mutations were also shown in cultures of mouse lymphoma L5178 TK+/- cells, and in human lymphoblasts at the thymidine kinase and 6-thioguanine loci hypoxanthine guanine phosphoribosyl transferase locus but not in Chinese hamster ovary (CHO) cells (CEPA, 1999). Both positive and negative results of sister chromatid exchange have been produced by acrylonitrile in both CHO cells and in human lymphoblasts in the presence of an activation system (TERA, 1997). Acrylonitrile induced sister chromatid exchange in human bronchial epithelial cells without the presence of S9 (TERA, 1997). Chromosome aberrations were observed in CHO cells by acrylonitrile in some *in vitro* studies (CEPA, 1999). Positive results have been observed in CHO cells in *in vitro* micronucleus assay studies (Woutersen, 1998). Acrylonitrile induced unscheduled DNA synthesis in primary rat liver hepatocytes but results were negative in human lymphocytes. Acrylonitrile induced DNA single-strand breaks in human bronchial epithelial cells, rat liver cells and calf thymus DNA (TERA, 1997). 2-Cyanoethylene oxide did not result in cell transformation of the *ras* oncogene in NIH3T3 cells (TERA, 1997).

Positive results have been observed in unscheduled DNA synthesis tests following administration of acrylonitrile by gavage in rats; however, results were negative in DNA repair and sister chromatid exchange in mice and rats following oral exposures (by gavage) (TERA, 1997). Except for an unscheduled DNA synthesis assay in rats, no mutagenic activity was observed *in vivo* either with chromosomal aberration or micronucleus assays in animal systems (Rabello-Gay and Ahmed, 1980).

Results of *in vitro* genotoxic studies with CEO were also mixed. Both positive and negative results have been observed in rat hepatocytes and rat HMEC. Positive results were reported for DNA single-strand breaks in calf thymus and pBR322 plasmid DNA (TERA, 1997). In two similar studies, CEO has been demonstrated to react with nucleotides of DNA *in vitro* to form adducts in TK6 lymphoblasts. It has been suggested that CEO induces DNA strand breaks and may interfere with DNA synthesis, and therefore may play a role in mutagenesis (TERA, 1997).

Recent genotoxic results of workers in a Hungarian Rayon plant, indicate that there may be *in vivo* genotoxic consequences in humans. The frequencies of chromosome aberrations, chromosome gaps and sister chromatid exchanges increased proportionally to the duration of exposure to acrylonitrile and/or dimethylformamide (Major et al., 1998). The fact that the factory air contained both acrylonitrile and dimethylformamide, raises some questions as to the impact of acrylonitrile by itself. However, this data does suggest a possible implication of acrylonitrile involvement.

3.5 Carcinogenicity

Long-term exposures to acrylonitrile through inhalation and oral routes have led to the development of tumours in animals. The common target organs are, the central nervous system (brain and spinal cord),

Zymbal gland, small intestine, forestomach and mammary gland (TERA, 1997). The data indicated a clear association between acrylonitrile exposure and cancer, with respects to, consistency in results from independent studies by different routes of exposure, positive dose-response indications for several tumour types and with statistically significant tumour incidences. The limitations of these studies are, only one species (i.e. rats) was studied and the predominant tumour types are rare in humans (e.g. astrocytomas in the brain, tumours in Zymbal gland and the forestomach).

Results obtained from epidemiological studies on exposed workers have been inconsistent. Increased mortality and/or incidence of lung and prostate cancers have been reported in some cohort studies whereas some follow-up studies and other studies do not provide similar results. Furthermore, two meta-analyses of combined data from 12 to 25 studies do not indicate an excess risk of mortality in exposed workers from all cancers, or specifically from respiratory cancer. The major deficiency in these human studies is the lack of reliable quantitative exposure data in dose-response assessment. The other confounding factor is that in most of the studies, there is a certain degree of co-exposure to other potential carcinogens (TERA, 1997; Collins and Acquavella, 1998).

In a retrospective epidemiology study of a fibers plant in the U.S. conducted by O'Berg (1980), 1,345 male textile workers exposed to low, medium and high concentrations of acrylonitrile, estimated as 11,000, 22,000 and 44,000 $\mu\text{g}/\text{m}^3$ were followed for more than 10 years. Twenty four cases of cancer were observed as compared with 19 expected. A significant increase in respiratory cancer was noted (e.g. 8 cases observed versus 4.1 expected), even when the contribution of smoking was taken into consideration (O'Berg, 1980). Three cases of prostate cancer were observed compared with 0.9 expected. There was an indication of increased cancer risk with increasing exposure duration. When a follow-up to the first study was published in 1985, again there was a marked increase in the number of lung cancer cases among those workers exposed to acrylonitrile (43 observed versus 36.7 expected) (O'Berg *et al.*, 1985). Though the increase in lung cancer incidence found in the follow-up study was not statistically significant, it found a significantly elevated prostate cancer rate (6 observed versus 1.5 expected).

In an analysis based on mortality, both the deaths related to the lung cancer and prostate cancer were statistically not significant. However, bladder cancer deaths were statistically significant, 3 observed versus 0.6 expected (O'Berg *et al.*, 1985). Results of a power analysis of the study suggest that, based on the size of the cohort, the study may not be sensitive enough to detect a significant increase in relative risk for lung cancer (O'Berg *et al.*, 1985; TERA, 1997).

Chen *et al.* (1987) studied 1,083 male workers at an acrylic fibers plant in the U.S. Potential exposure was classified into low, moderate and high exposure groups. In the high exposure group, there were 18 cancer deaths compared with 20.4 expected; of these, 5 were lung cancer deaths versus 7.6 expected. Based on exposure level or cumulative exposure index, no differences were observed between

observed and expected numbers. Four cases of prostate cancer were observed compared with 0.9 expected. This excess cancer risk was statistically significant and occurred in workers in the high exposure group, with over 20 years of exposure.

Male workers from two cohorts were studied for acrylonitrile exposures (Collins *et al.*, 1989). Four exposure categories were established based on industrial hygiene monitoring done in 1977 and assumed to represent levels at the plant start up. Exposures were defined as: none; 0.01 to 0.7 ppm/year (22 to 1500 $\mu\text{g}/\text{m}^3$ per year); 0.7 to 7 ppm/year (1500 to 15000 $\mu\text{g}/\text{m}^3$ per year); and >7 ppm/year (>15000 $\mu\text{g}/\text{m}^3$ per year). A total of 1774/2671 workers were considered exposed (i.e. a cumulative exposure of over 0.01 ppm/year). Forty three cancer deaths were observed with a standardized mortality ratio (SMR) of 1.01. Among these, 15 lung cancer deaths were reported (SMR = 1.0). Two deaths were from prostate cancer (SMR = 1.49). These results were similar to those of the non-exposed workers.

A retrospective cohort of eight companies in The Netherlands was studied by Swaen *et al.* (1992). Workers studied had exposures over 20 years. Exposure concentrations were estimated based on both an 8-hour time-weight-average and on job classifications: 0-0.5 ppm (0-1085 $\mu\text{g}/\text{m}^3$), 0.5-1 ppm (1085-2170 $\mu\text{g}/\text{m}^3$), 1-2 ppm (2170-4340 $\mu\text{g}/\text{m}^3$) and 2-5 ppm (4340-10850 $\mu\text{g}/\text{m}^3$). Peak exposures (<10 ppm, 10-20 ppm, 20-30 ppm) were also evaluated in this study. There were 42 observed cancer deaths compared with 50.8 expected; of these, 16 were trachea and lung cancer deaths compared with 19.5 expected and 2 prostate cancer deaths compared with 1.22 expected. In the non-exposed group, the SMR for all cancers and for cancers of the trachea and lung were similar to the those of the exposed cohort. However, for prostate cancer, there were 6 observed death compared with 10 expected in the non-exposed cohort. The authors suggested that acrylonitrile may not be a human carcinogen at concentrations occurred in the Dutch chemical industry.

Statistically significant increases in cancer incidence were also noted in two other epidemiology studies. Delzell and Monson (1982) noted a significant increase in lung cancer among rubber manufacturing plant workers, though exposure levels were not determined nor were smoking and exposure to other potential carcinogens taken into consideration. Thiess *et al.* (1980) observed a significant increase in lung and lymph system cancers in workers in a German acrylonitrile processing plant.

Werner and Carter (1981) reported an excess in total cancer deaths (stomach and lung cancers) among workers in an acrylonitrile polymerisation and acrylic fibre spinning plant, but the increase was not statistically significant. In contrast to the findings of these studies, seven other studies reported no evidence of carcinogenic risk from acrylonitrile exposure (WHO, 1983). All of the studies, however, suffer from inadequate consideration of the variables, methodological difficulties, or inadequate exposure information regarding acrylonitrile or other carcinogens (WHO, 1983; 1987). Four recent epidemiological studies from cohorts in the U.K., The Netherlands and the U.S.A. did not establish a

causal relationship between occupational acrylonitrile exposure and increased cancer mortality (Benn and Osborne, 1998; Blair *et al.*, 1998; Swaen *et al.*, 1998; Wood *et al.*, 1998). Most of these studies suffer from limiting factors which have been experienced in previous studies. These limitations include, a lack of information on workers' smoking habits, limited estimates of acrylonitrile exposure and relatively small size of the cohorts (Benn and Osborne, 1998; Swaen *et al.*, 1998; Wood *et al.*, 1998). In the study performed by the National Cancer Institute, even though workers smoking habits were factored in, exposure concentration was monitored and a rather large number of acrylonitrile plants involving over 25,460 workers were also included, such causal relationship was still not observed (Blair *et al.*, 1998). In a few situations, a higher, but not statistically significant lung cancer mortality was observed. However, there was no consistent trend to establish a dose-response relationship (Benn and Osborne, 1998; Blair *et al.*, 1998).

There are only a few inhalation studies available to assess the carcinogenicity of acrylonitrile in animals. A detailed two-year inhalation carcinogenicity study was conducted in Sprague-Dawley rats (100/sex/group) exposed to 0, 20, 80 ppm (0, 44,000 and 174,000 $\mu\text{g}/\text{m}^3$) of acrylonitrile for 6 hours/day, 5 days/week for two years (Quast *et al.*, 1980a). Non-neoplastic effects observed included inflammatory and degenerative changes in the nasal turbinates and the central nervous system. These changes were particularly prevalent and more intense in the 80 ppm group and likely attributed to the irritation of acrylonitrile. Statistically significant increases in tumour incidence were noted in male and female rats. The tumours observed were those of the central nervous system (astrocytomas; statistically significant for the 20 and 80 ppm dose groups), Zymbal gland (statistically significant for the 80 ppm group only), tongue (statistically significant for the 80 ppm group only), small intestine (statistically significant for the males in the 80 ppm group only), and mammary gland (only if adenocarcinoma was considered for the increase; no difference between control and exposed animals was observed if all mammary tumours were considered). Some animals were exposed to acrylonitrile for a little less than two years because animals had to be sacrificed due to the appearance of large mammary gland tumours (ATSDR, 1990; US EPA 1983; US EPA, 1999a). In addition, in a long-term carcinogenicity bioassay, Maltoni *et al.* (1988) observed tumours in the liver of rats. There are no data in the literature for an inhalation bioassay performed in a species other than the rat.

Similar results of statistically significant increases in tumour incidence were observed following treatment of Sprague-Dawley and Fischer 344 rats to acrylonitrile by the oral route of exposure (Quast *et al.* 1980b; Biodynamics, 1980).

Caution should be exercised when attempting extrapolation of the predominant acrylonitrile-induced CNS tumour (astrocytoma) incidence which has occurred in rats to humans (TERA, 1997). No acrylonitrile-related excess brain cancer risk was reported in any of the epidemiology studies. In fact, brain cancer deaths were reported to be lower in the exposed than in the non-exposed groups in some studies (Collins *et al.*, 1989; Swaen *et al.*, 1992; Wener and Carter, 1981). In a retrospective study

of mortality in workers exposed to acrylonitrile in various industries in The Netherlands, slightly higher brain cancer deaths were found; however, no brain tumour deaths were noted in the high exposure group (Swaen *et al.*, 1998). The absence of a dose-effect characteristic argues against a causal relationship between brain tumour death and acrylonitrile exposure. It has been suggested that humans have a pathway for the detoxication of acrylonitrile which is absent in rodents, and this may render humans to be less sensitive to acrylonitrile carcinogenicity than animals (TERA, 1997). As well, acrylonitrile carcinogenicity has not been reported in animal species other than the rat. However, there are no data available to suggest that acrylonitrile-induced tumourigenic events do not occur in other animal species.

Based on the consistence in acrylonitrile-induced cancer incidences in rats, a clear causal relationship exists between exposure and the various types of tumours through both oral and inhalation routes of exposure, possible mutagenic effects of acrylonitrile and its oxidative metabolite (2-cyanoethylene oxide) in both human and rat tissues. In addition a causal relationship does exist between available human carcinogenicity data for increased lung and prostate cancer mortality in some cohorts, though these increases are not dose-related and do not reach a statistically significant level. Therefore, the carcinogenic potential of acrylonitrile to humans cannot be ruled out.

Considering sufficient evidence in animals and some evidence in humans, various agencies have classified acrylonitrile as a potential carcinogen. The US EPA (1999) considers acrylonitrile to be a probable human carcinogen (class B1) based on the observation of a significant increase in the incidence of lung cancer in exposed workers and on the observation of tumours in rats exposed either by inhalation or oral routes. The International Agency for Research on Cancer (IARC) also classified acrylonitrile as a probable human carcinogen (group 2A) based on sufficient evidence for animals, but with limited carcinogenic evidence for humans. The ACGIH (1991) has given acrylonitrile a suspected human carcinogen classification on the basis of carcinogenicity in animals with data showing relevance to worker exposure, and conflicting or insufficient epidemiological studies for cancer in exposed humans.

3.6 Environmental Effects

Toxicity data for wildlife species are not available in the literature. Studies of 13 insect species found that LC_{50} values for these insects ranged from 1.1×10^5 to $3.7 \times 10^7 \mu\text{g}/\text{m}^3$ (CEPA, 1999). A fifty percent decrease in progeny was reported in rice weevil (*Sitophilus oryzae* L.) as the result of 8-hour exposures to $4.0 \times 10^5 \mu\text{g}/\text{m}^3$ acrylonitrile (Rajendran and Muthu, 1981). The rice weevil was the most sensitive of the insect species studied as 4-hour exposures to 1×10^6 to $1.5 \times 10^6 \mu\text{g}/\text{m}^3$ acrylonitrile resulted in 100% mortality (Rajendran and Muthu, 1977).

Environment Canada reviewed numerous aquatic toxicity studies for its Priority Substances List Assessment Report of acrylonitrile and concluded that acrylonitrile was moderately toxic to fish and amphibians as 96-hour LC_{50} values range from 10 to 20 mg/L (CEPA, 1999). The US EPA has not set criteria for the protection of aquatic life. It reports an acute lowest effect concentration (LEC) in freshwater organisms of 7.6 mg/L and a chronic LEC of 2.6 mg/L. A 28-day study in bluegill sunfish showed a half-life of 4 to 7 days.

Studies conducted in China on the toxicity of acrylonitrile to duckweed (*Lemna minor* L.) determined a 96-hour no-observed-effect concentration (NOEC) of 6.2 mg/L and a 96-hour lowest-observed-effect concentration (LOEC) of 12.5 mg/L for inhibition of plant growth (Zhang, 1997).

Acrylonitrile concentrations of up to 5,000 mg/L do not appear to be toxic to bacterial species as acrylonitrile is readily degraded (Wenzhong et al, 1991). Applications of 1,000 μ g/g acrylonitrile to soil were found to affect soil microbes as decreased soil respiration was observed over a monitoring period of 6 days (Walton et al, 1989).

4.0 Existing Air Quality Criteria

4.1 Overview

The current Ontario 24-hour Ambient Air Quality Criterion (AAQC) for acrylonitrile is 100 μ g/m³ and the half-hour point of impingement (POI) guideline is 300 μ g/m³. The basis for both criteria was protection of human health (MOEE, 1994a).

In revising the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments, and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency specific summaries of information guidelines for acrylonitrile are presented in Section 11.0 of this report. A brief summary is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations to half-hour POI standards and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term

exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Most of the agencies reviewed have developed long-term ambient air quality criteria with basis based on the carcinogenic and non-carcinogenic properties of acrylonitrile.

The US EPA has established an inhalation cancer unit risk of 6.8×10^{-5} per ($\mu\text{g}/\text{m}^3$) for lifetime exposure to acrylonitrile. That is, for a lifetime exposure to this chemical at an ambient air concentration of $0.01 \mu\text{g}/\text{m}^3$, the probability of a cancer incidence is one in a million. Agencies, such as, New Jersey, Massachusetts, Michigan and New York have adopted the assessment and unit risk estimate from the US EPA to derive their long-term guidelines. California developed its own cancer unit risk estimate which resulted in a more conservative guideline. The WHO established its cancer unit risk estimate based on the same epidemiological study used by the US EPA, but employed a different method of calculation and resulted in a unit risk of 2×10^{-5} per ($\mu\text{g}/\text{m}^3$).

The US EPA has also developed an inhalation reference concentration (RfC) of $2 \mu\text{g}/\text{m}^3$ based on lung cell hyperplasia in rats. The states of California, Massachusetts, Michigan and New Jersey have adopted the RfC of the US EPA for their criteria derivation. The short-term guideline concentration of the State of New York was derived from the occupational exposure limits developed by the US National Institute for Occupational Health and Safety (NIOSH).

Table 1. Summary of Existing Air Quality Guidelines¹ for Acrylonitrile

Agency	Guideline Value ²	Basis of Guideline	Date ³	Comments
USEPA (IRIS)	2 µg/m ³ (inhalation reference exposure level)	2-yr rat inhalation, Lung cell hyperplasia	1991	LOAEL (HEC) adjusted with uncertainty factors
	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1992	1*10 ⁻⁴ additional cancer risk
	0.1 µg/m ³ (lifetime exposure)	unit risk 6.8 x 10 ⁻⁵ per µg/m ³		1*10 ⁻⁵ additional cancer risk
California (CAPCOA)	1 µg/m ³ (lifetime exposure)			1*10 ⁻⁴ additional cancer risk
	2 µg/m ³ (chronic annual)	Respiratory and skin irritation	1993	Non-cancer Reference Exposure Level (Chronic annual); IRIS
	0.003 µg/m ³ (lifetime exposure)	Lung cancer in humans	1996	1*10 ⁻⁴ additional cancer risk
		unit risk 2.9 x 10 ⁻⁴ per µg/m ³		
Massachusetts	0.4 µg/m ³ (24-hour average)	Lung cell hyperplasia	1995	Threshold and non-threshold effects
	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1991	1*10 ⁻⁴ additional cancer risk
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
Michigan	2 µg/m ³ (24-hour average ITSL)	Lung cell hyperplasia	1991	Screening level for a 24-hour averaging time
	0.01 µg/m ³ (lifetime exposure)	Lung cancer in humans	1987	Annual average IRSRL; US EPA
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
New Jersey	2 µg/m ³ (annual average)	Lung cell hyperplasia	1994	Ambient annual guideline concentration, annual average
	0.01 µg/m ³ (lifetime exposure - based on IRIS)	Lung cancer in humans	1994	1*10 ⁻⁴ additional cancer risk; US EPA carcinogen class: B1
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
New York	220 µg/m ³ (1-hour average - SGC)	Occupational exposure limits	1994	Acute 1-hour average; based on NIOSH REL-TWA
	0.01 µg/m ³ (annual - AGC)	Lung cancer in humans	1994	Chronic annual; 1*10 ⁻⁴ additional cancer risk; US EPA
		unit risk 6.8 x 10 ⁻⁵ per µg/m ³		
WHO	0.05 µg/m ³ (lifetime exposure)	Lung cancer in humans and rats	1987	1*10 ⁻⁴ unit cancer risk
	0.5 µg/m ³ (lifetime exposure)	unit risk 2 x 10 ⁻⁵ per µg/m ³		1*10 ⁻⁵ unit cancer risk
The Netherlands	1 µg/m ³ (Annual average)	Basis not available	1992	Basis not available
	0.1 µg/m ³ (lifetime exposure)	Basis not available	1992	1*10 ⁻⁴ additional cancer risk (target value)
Sweden	none		1993	No value found
Canada (CEPA)	0.12 µg/m ³ (lifetime exposure)	TC ₀₁ of 6000 µg/m ³ divided by 50000 and 5000 respectively	1999	PSL2 assessment based on TC ₀₁ of 6000 µg/m ³ for female rats
Ontario	1.2 µg/m ³ (lifetime exposure)			
	100 µg/m ³ (24 hour average)	Health	1994	24-hour averaging time: Ambient Air Quality Criteria
	300 µg/m ³ (POI; half-hour))	Health	1985	Point Of Impingement guideline

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations
- As different jurisdictions use different units to express concentration, when necessary a conversion factor of 1 ppm = 2203 µg/m³ was used.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

The Netherlands uses its MIC (Maximum Immission Concentration) of $1 \mu\text{g}/\text{m}^3$ as an annual average limit value for acrylonitrile by applying a factor of 1000 for carcinogens to the MAC (Maximum Acceptable Concentration), and adjusting for the odour threshold with a factor of 10. It has also set as a long-term target value of $0.1 \mu\text{g}/\text{m}^3$ for lifetime exposure.

Environment Canada and Health Canada have listed acrylonitrile as a priority chemical (PSL2) for risk assessment under the *Canadian Environmental Protection Act* (CEPA, 1999). A Tumourigenic Concentration at a 5% increase in incidence or mortality (TC_{05}) of $6 \text{ mg}/\text{m}^3$ has been proposed. The application of a margin of safety factor of 5000 and 50000 will provide protection to that is comparable to the range for low dose risk estimates generally considered by various agencies to be "essentially negligible", i.e. 10^{-5} and 10^{-6} respectively (Health Canada, 1996).

Workplace exposure limits have been established by different agencies. The Occupational Safety and Health Administration (OSHA) has set the legal airborne PEL-TWA (Permissible Exposure Limit - Time Weighted Average) at $4,400 \mu\text{g}/\text{m}^3$ over an 8-hour work shift, and the ceiling, or the limit not to be exceeded during any 15-minute work period, at $22,000 \mu\text{g}/\text{m}^3$. The NIOSH has set a REL-TWA (Recommended airborne Exposure Limit - Time Weighted Average) of $2,200 \mu\text{g}/\text{m}^3$, and $22,000 \mu\text{g}/\text{m}^3$ as the limit not to be exceeded during any 15-minute work period (NIOSH 1994, 1988b). The American Conference of Governmental Industrial Hygienists (ACGIH) has set a TLV-TWA (Threshold Limit Value - Time Weighted Average) at $4,400 \mu\text{g}/\text{m}^3$ (ACGIH, 1991). Acrylonitrile also carries an OSHA and ACGIH skin notation, as dermal exposure can result in systemic effects. The US Department of Health and Human Services calculated an acute (14-day) inhalation minimum risk level (MRL) of 1.5 ppm ($325 \text{ mg}/\text{m}^3$), based on a study showing neurological effects in workers (Jakubowski et al. 1987, as cited in ATSDR, 1990).

4.2 Evaluation of Existing Criteria

Most of the acute effects of acrylonitrile exposure resemble symptoms of cyanide poisoning, such as the CNS effects of headache, nausea, vertigo and convulsion and effects of the liver. Acute exposure of rats induces irritation caused directly by acrylonitrile, and respiratory effects by cyanide poisoning resulting from the breakdown of CEO. Most of the agencies reviewed do not have criteria developed based on the acute effects of acrylonitrile. The short-term criteria of New York was derived from an occupational exposure limit (TLV-TWA), whereas the 24-hour ITSL of Michigan was adopted from the chronic RFC of the US EPA.

Information on the adverse systemic effects of long-term or chronic exposure to acrylonitrile was primarily obtained in studies designed for carcinogenicity bioassays. Except the inflammatory changes observed in the nasal turbinates, non-cancerous changes observed generally involved the hyperplastic alterations in the CNS and the respiratory epithelium. Furthermore, neurophysiological changes in

motor and sensory conduction have also been reported. Other systemic effects include necrosis of the adrenal gland and the gastrointestinal tract, liver, kidney, lung. Most of the U.S. agencies adopted the RfC developed by the US EPA for their long-term non-carcinogenic air quality guidelines. All the agencies reviewed consider the acrylonitrile-induced cancer effect as the most sensitive endpoint and have developed carcinogenicity-based air quality guidelines. The approaches of developing air quality standards based on carcinogenic and non-carcinogenic effects will be examined in the following.

Criteria Based on Carcinogenicity

In general, all the U.S. agencies reviewed have adopted or derived their values from the inhalation lifetime cancer risk estimate developed by the US EPA (US EPA, 1999a). The data used for the estimate was obtained from the retrospective cohort epidemiology study for increased lung cancer incidence in humans (O'Berg, 1980). Male textile workers, exposed to low, medium and high concentrations, estimated as 11,000, 22,000 and 44,000 $\mu\text{g}/\text{m}^3$ of acrylonitrile, were followed for at least 10 years. A significant increase in respiratory cancer was noted, even when the contribution of smoking was taken into consideration (O'Berg, 1980).

The US EPA used the average relative risk model to calculate the inhalation unit risk of 6.8×10^{-5} ($\mu\text{g}/\text{m}^3$)⁻¹; a lifetime exposure to 0.01 $\mu\text{g}/\text{m}^3$ of acrylonitrile is estimated to result in an additional cancer risk to humans of 1 in 1,000,000. The US EPA considers that the cohort in the study of O'Berg (1980) was sufficiently large and was followed for an adequate period. A dose-response relationship for the increased cancer risk was observed. Furthermore, the increased risk remained after adjustment for smoking. The exposure levels of 5 to 20 ppm (11 to 44 mg/m^3) were estimated by company representatives (US EPA, 1999a).

The US EPA has also derived an inhalation cancer unit risk of 1.5×10^{-5} ($\mu\text{g}/\text{m}^3$)⁻¹ based on the animal data of Quast, *et al.* (1980a). This cancer unit risk is within an order of magnitude of the unit risk estimate based on the human data of the study of O'Berg (1980). This finding appears to lend support to the carcinogenic classification for acrylonitrile. However, the significance of tumours found in experimental animals is unknown. For example, some tumour incidences in animals include those located in the Zymbal gland and the forestomach, two anatomical features not found in humans.

Using the same rationale used by the US EPA, Massachusetts, Michigan, New Jersey, and New York consider 0.01 $\mu\text{g}/\text{m}^3$ to be their annual exposure limit. California modified the US EPA unit risk to the upper 95% bound, and considered 70 years rather than 60 years for the duration of exposure. This resulted in a unit risk of 2.9×10^{-4} per $\mu\text{g}/\text{m}^3$ acrylonitrile. That is, exposure to 0.003 $\mu\text{g}/\text{m}^3$ would result in an estimated one in a million excess cancer risk (OEHHA, 1997a).

The WHO (1987) considers acrylonitrile as if it were a human carcinogen based on its carcinogenicity in animals because of the limited evidence of carcinogenicity in humans. Using the average relative risk model, a value for unit risk was determined to be 1.7×10^{-5} per ($\mu\text{g}/\text{m}^3$) for acrylonitrile (WHO, 1987).

The WHO (1987) found this value consistent with the lifetime inhalation risk derived from animal studies in the 1983 US EPA Health Assessment Document. The WHO does not recommend a safe level for acrylonitrile, and concludes that at $1 \mu\text{g}/\text{m}^3$ the lifetime risk is about 2×10^{-5} . This represents an additional cancer risk to humans of 1 in 1,000,000 over a lifetime exposure to $0.05 \mu\text{g}/\text{m}^3$.

Acrylonitrile has elicited genotoxic properties in several *in vitro* and *in vivo* studies using animal and human tissues. Furthermore, toxicologists at TERA suggested that non-carcinogenic effects of acrylonitrile do not appear to be a prerequisite for the carcinogenic toxicity of this compound (TERA, 1997). Therefore, acrylonitrile is considered to be a non-threshold carcinogen by both the US EPA and the IARC, and more recently by TERA and the Canadian federal government.

The lack of a clear human carcinogenicity picture has led toxicologists at the Toxicology for Excellence in Risk Assessment (TERA) to suggest that acrylonitrile's human carcinogenic classification must be re-evaluated as the current classification may no longer be supportable (TERA, 1998). The TERA has decided to employ data from an animal inhalation study to derive its cancer risk slope factor for acrylonitrile. Their reasoning for this is based on: results from epidemiological studies are equivocal; available human studies have methodological limitations, such as a lack of reliable exposure information and co-exposure to other potential carcinogens; the power of these studies is low to detect a statistically significant cancer risk in exposed workers; and the results of meta-analyses of data from many epidemiological studies did not indicate a causal relationship between occupational exposure to acrylonitrile and subsequent death from respiratory cancer. On the other hand, animal data provide a consistence of acrylonitrile-induced cancer incidences in the rats and a clear causal relationship between exposure and the various types of tumours through both oral and inhalation routes of exposure (TERA, 1997).

The inhalation study of Quast *et al.* (1980a) was chosen as the primary source of data. In the absence of a biologically-based model to extrapolate experimental exposure concentrations to human equivalent exposure concentrations, as recommended by the US EPA in its recently Proposed Guidelines for Carcinogen Risk Assessment (US EPA, 1996), the methods developed by the US EPA to calculate human equivalent concentrations (HEC) in the derivation of the reference concentration (RfC) was used. The human equivalent concentrations of 0, 7.5 and $30 \text{ mg}/\text{m}^3$ were derived from the exposure concentrations of 0, 20 and 80 ppm in the animal study. Of the four target organs examined, analysis has been focussed on the modelling of the astrocytomas, which have the most consistent occurrence across studies and exposure routes. The Zymbal gland is not a comparable target organ in humans, and tumours of the tongue and the small intestine were not observed by the oral route of exposure.

The astrocytoma data have been adjusted for early mortality (this was not indicated in the US EPA's assessment based on the same study), and a linear extrapolation (polynomial model) method has been employed to perform the analysis. Based on the US EPA's proposed guidelines (US EPA, 1996) the ED₁₀ (effective dose at 10% increase in tumour incidence) was calculated to be 14.55 and 12.18 mg/m³ and the LED₁₀ (95% lower confidence limit of the ED₁₀) to be 9.09 and 9.11 mg/m³ for the male and the female rats respectively. Accordingly, the slopes (slope = 0.1 / ED₁₀ or LED₁₀) were calculated to be 0.0069 per mg/m³ ($6.9 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) and 0.0082 per mg/m³ ($8.2 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) based on ED₁₀ and, 0.011 per mg/m³ and 0.011 per mg/m³ ($1.1 \times 10^{-6} \cdot (\mu\text{g}/\text{m}^3)^{-1}$) based on the LED₁₀ for the male and female rats, respectively. The risk specific concentrations (calculated as excess risk = slope x [acrylonitrile] in mg/m³) for the female were slightly greater than those of the male rats. It was determined that for the female rats, based on the ED₁₀, the risk specific concentrations were:

10⁻⁴ risk: 12 µg/m³
10⁻⁵ risk: 1.2 µg/m³
10⁻⁶ risk: 0.12 µg/m³

based on LED₁₀, the risk specific concentrations were:

10⁻⁴ risk: 9 µg/m³
10⁻⁵ risk: 0.9 µg/m³
10⁻⁶ risk: 0.09 µg/m³.

The TERA suggests that this cancer potency may represent an overestimation of actual risk to humans (TERA, 1997) because: it is considered that the astrocytoma is rare in humans; the conversion of an intermittent exposure dosage to continuous regime also results in an overestimation of risk; and the detoxication mechanism for acrylonitrile in humans may be more efficient than rodents and this renders humans to be less sensitive than animals to acrylonitrile carcinogenicity.

Acrylonitrile is listed as a priority chemical (PSL2) for risk assessment under CEPA (CEPA, 1999). In agreement with most agencies reviewed, Environment Canada and Health Canada consider cancer the critical endpoint for quantitative dose-response risk assessment. The inhalation study of Quast *et al.* (1980a) has been chosen as the key source for quantitative data and astrocytoma of the CNS has been considered the most appropriate tumour type for cancer risk estimation. Environmental Canada and Health Canada consider that acrylonitrile-induced carcinogenesis may not be unique to rats and suggest that based on PB-PK modelling predictions, cyanoethylene oxide in the brains of humans would be considerably higher than those in rats exposed to similar concentrations of acrylonitrile. The lack of evidence of brain tumours in epidemiological studies may be attributable to the limited power to detect the excess of rare brain tumours (CEPA, 1999). In their assessment, both benign and malignant

tumours of the astrocytoma type in the CNS were combined for the calculation, using a multistage model (GLOBAL 82). Tumour incidences have been adjusted to exclude animals dying before six months (prior to observation on the first tumour). Dose scaling between animals and humans was considered because of the difference in inhalation volume and body weight, based on the averaged breathing volume of 0.11 m³ air/day for a 0.35 kg rat and 23 m³/day for a 70 kg adult human.

The tumourigenic concentration at 5% increase in incidence or mortality (TC₀₅) for the combined tumour incidence of tumours in the brain and the spinal cord in female rats is estimated to be 6000 µg/m³ (8900 µg/m³ for the male rats). This is the lowest TC₀₅ (human equivalent value). The lower 95% confidence limit is 4500 µg/m³. The application of a margin of safety factor of 5000 and 50000 to the TC₀₅ will provide protection that is associated with the range for low dose risk estimates generally considered by various agencies to be "essentially negligible", i.e. 10⁻⁵ and 10⁻⁶ respectively (Health Canada, 1996). Thus, at an exposure concentration of 1.2 µg/m³ for a lifetime, the likelihood of tumour incidence is one in a hundred thousand. This value is in close agreement with the risk specific concentration at an equivalent risk level based on the ED₁₀ for female rats as estimated by TERA.

Criteria based on non-cancer end points

The non-carcinogenic end-point for injury to the nasal respiratory epithelium in rats, based on the inhalation study of Quast *et al.* (1980a), was employed by the US EPA to calculate a Reference Concentration (RfC) of 2 µg/m³ for acrylonitrile. Sprague-Dawley rats were exposed to 0, 44,000 or 174,000 µg/m³ of acrylonitrile for two years. A dose-dependent, and statistically significant increase in degenerative and inflammatory changes in the respiratory epithelium and nasal turbinates was observed with the acrylonitrile-treated animals. The RfC was calculated from an inhalation LOAEL-HEC (Lowest Observed Adverse Effect Level - Human Equivalent Concentration) by the application of a total uncertainty factor of 900: 10 for the protection of sensitive individuals; 3 to adjust from a minimally adverse LOAEL to a NOAEL; 3 for interspecies variability; and 10 for deficiencies in the database). The overall confidence in the RfC was given as medium to low. Though the study on which the RfC was based was well conducted, it involved only one species and it did not identify a NOAEL. There are a lack of chronic or subchronic data in a second species, and a lack of reproductive data via inhalation, while an oral study showed reproductive effects.

Michigan and New Jersey have adopted the US EPA RfC of 2 µg/m³ for their air quality criteria based on a 24-hour average period. California has adopted the US EPA RfC as its chronic reference exposure Level (REL).

New York (1994) classifies acrylonitrile as a contaminant with high toxicity. It derived a Short-term Guideline Concentration (SGC; 1-hour) of 220 µg/m³ by applying an uncertainty factor to the REL-TWA of 2,200 µg/m³ of the NIOSH. NIOSH (1988,1997) notes that since acrylonitrile is a potential

carcinogen, the REL-TWA of 1 ppm (2,200 $\mu\text{g}/\text{m}^3$) is based on the lowest feasible concentration. The US Department of Health and Human Services calculated an acute (14- day) inhalation minimum risk level (MRL) of 1.5 ppm (3250 $\mu\text{g}/\text{m}^3$) based on a study showing neurological effects in workers (Jakubowski et al. 1987, as cited in ATSDR, 1990).

5.0 Responses of Stakeholders to the Information Draft

In January, 1999 the Ministry posted information draft documents for eighteen chemicals, including acrylonitrile, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; the appropriateness of considering the carcinogenicity of acrylonitrile as the most sensitive endpoint; and, any technical or economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received three submissions from various stakeholders regarding the draft document for acrylonitrile. A rubber industry stakeholder commented that it would be possible to meet a revised standard at a value of an order of magnitude (10-fold) lower than that of the current interim POI standard and further reductions may be achieved by applying additional control technology. Comments from a utility stakeholder indicated that the release of acrylonitrile from their facility was almost negligible. One federal government agency suggested that, where possible, information regarding the releases and uses of acrylonitrile specific to Canada and Ontario should be used.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide additional information such as any technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for acrylonitrile. If the proposed standard cannot be achieved immediately, this phase will be followed by a third phase in which risk management options will be

discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for Acrylonitrile

The current Ambient Air Quality Criterion (AAQC) for acrylonitrile in Ontario is $100 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time. The half-hour POI guideline is $300 \mu\text{g}/\text{m}^3$. These criteria were established based on the adverse health effects of acrylonitrile.

Inhalation of acrylonitrile through acute exposures may result in central nervous system effects such as headache, vertigo, nausea, and convulsion. In animals, acute inhalation exposure may induce toxicity resembling cyanide poisoning which includes respiratory irritation, inflammatory and degenerative changes in the respiratory epithelial tissues, as well as central nervous systems dysfunction. Chronic exposure induces necrosis to liver, lungs, kidney, the central nervous system and respiratory tissue damage. All six of the U.S. agencies reviewed have developed air quality criteria based on the adverse effects of acrylonitrile on respiratory tissues.

There is evidence that acrylonitrile may be genotoxic. This is supported by positive mutagenic assay results observed in some bacteria, animal and human cells *in vitro*, despite *in vivo* study results which are less consistent. It is also suggested that non-carcinogenic effects of acrylonitrile do not appear to be a prerequisite for the carcinogenic effect of this compound.

The most sensitive endpoint of chronic acrylonitrile exposure is the development of cancer. In rats, it has been consistently demonstrated that chronic exposure to acrylonitrile through the inhalation and oral routes induces cancer. Tumours in the brain, spinal cord, and Zymbal gland are the most common tumour types found in rats. Results from human studies based on available epidemiological data are less consistent as the Zymbal gland is not found in humans, as such, similar brain tumours have not been reported in workers at acrylonitrile plants. Lung and prostate cancers have been found to be associated with exposure to acrylonitrile in workers in some cohorts. Unfortunately, follow-up studies always fail to confirm the significance of these findings. The major deficiency in these human studies is the lack of reliable quantitative exposure data in dose-response assessment. Furthermore, in these studies, workers were often co-exposed to certain other carcinogens that existed in the plant.

In spite of the uncertainties in the data concerns about the carcinogenic potential of acrylonitrile have led to the development of cancer-based exposure limits by most agencies. These agencies suggest that exposure to air concentrations of acrylonitrile in the range of 0.003 to 0.12 $\mu\text{g}/\text{m}^3$ over a lifetime may result in an additional cancer risk of one in a million.

The scientific rationale and the risk assessment for the TC_{05} of Environment Canada and Health Canada are supported by a recent independent risk assessment performed by TERA and by a group of panel toxicologists of TERA. Thus, the TC_{05} is considered the most appropriate basis for the development of air quality standards for acrylonitrile in Ontario. The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$, respectively. These values are in close agreement with the risk-specific concentration of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$ (at lifetime exposure cancer risk levels of one in a hundred thousand and one in a million, respectively), derived based on the ED_{10} for female rats, as estimated by TERA.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide and the science upon which these standards are based. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepts the scientific rationale and risk assessment employed by Environment Canada and Health Canada to develop their TC_{05} values for the tumourigenic (tumour causing) effect of acrylonitrile. The application of margin of safety factors of 5,000 and 50,000 to the TC_{05} produces risk concentrations of 1.2 and 0.12 $\mu\text{g}/\text{m}^3$, representing excess cancer risk of 1 in 100,000 and 1 in 1,000,000, respectively.

In general, the Ministry strives to manage exposure to carcinogens down to a risk represented by no more than 1 excess cancer in 1,000,000. This is consistent with the Ministry's approach to carcinogenic risk management for other environmental exposures (e.g., drinking water and contaminated sites) and with other jurisdictions, in particular throughout the United States. As a result, the Ministry proposes to derive an annual AAQC based on the risk specific concentration of 0.12 $\mu\text{g}/\text{m}^3$.

The Ministry of the Environment normally uses a factor of 15 to derive half-hour POI standards and guidelines from criteria based on annual average concentrations and a factor of 3 to derive POIs from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for acrylonitrile:

- an annual average AAQC of $0.12 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound; and,
- a 24-hour average AAQC of $0.6 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile based on the carcinogenic effect of this compound.

Based on supporting science and dispersion modelling, a half-hour POI standard of $1.8 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $300 \mu\text{g}/\text{m}^3$ to this revised level of $1.8 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- $1.8 \mu\text{g}/\text{m}^3$ to $180 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for acrylonitrile; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the

submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of

cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;

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- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>*

Comments relevant to the setting of air quality standards for acrylonitrile can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. The reference concentration for chronic inhalation exposure (RfC) is $2 \mu\text{g}/\text{m}^3$ (US EPA, 1999a; last review 08/15/91).

Acrylonitrile is classified as a probable human carcinogen (B1) with a unit risk from inhalation exposure of 6.8×10^{-5} per $(\mu\text{g}/\text{m}^3)$.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and development, Washington, D.C., U.S.A.

Key Reference(s):

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6. Peer Review Process and Public Consultation:

US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

No current guidelines exist for acrylonitrile.

8. Key Risk Assessment Considerations:

The US EPA (1999) has calculated an RfC which represents risk from adverse effects other than cancer. This RfC was calculated using results from a 2-year rat inhalation study (Quast *et al.*, 1980). Rats were exposed to 0, 7,700 and 31,000 $\mu\text{g}/\text{m}^3$ of acrylonitrile for 6 hours/day, 5 days/week for 2 years. In the high dose group, a statistically significant increase in mortality was noted in the first year for rats of both sexes. In the lower dose group, female rats were sacrificed early due to the occurrence of

large, benign, mammary gland tumours. This sacrifice during the last 10 weeks of the study was due to an increase in the onset, occurrence and size of spontaneously occurring tumours. Gross and histopathological evaluation showed exposure-related adverse effects to the nasal respiratory epithelium and the brain. The incidence of glial cell tumours (astrocytomas) was significantly increased in both male and female rats at the high dose level (31,000 $\mu\text{g}/\text{m}^3$). The NOAEL(HEC) and the LOAEL(HEC) for non-carcinogenic, extra-respiratory effects are 7,700 $\mu\text{g}/\text{m}^3$ and 31,000 $\mu\text{g}/\text{m}^3$, respectively. An inhalation uncertainty factor of 1000 (10 for the protection of unusually sensitive individuals; 3 for the adjustment from a minimally adverse LOAEL to a NOAEL; 3 for interspecies variability, and 10 due to an incomplete database, specifically, the lack of inhalation data in a second species) was used to arrive at the RfC of 2 $\mu\text{g}/\text{m}^3$. The inhalation RfC is rated medium in confidence predominantly because it was based on a study using only one species.

For the cancer risk assessment, the average relative risk dose extrapolation method was used to calculate a unit risk from inhalation exposure of 6.8×10^{-5} per $\mu\text{g}/\text{m}^3$ based on results from O'Berg (1980). This is equivalent to an estimated excess cancer risk of 1 in 10^6 for lifetime exposure to 0.01 $\mu\text{g}/\text{m}^3$ of acrylonitrile.

Several epidemiology studies have examined the morbidity and mortality of workers exposed to acrylonitrile. In the O'Berg (1980) study, a trend of increased cancer incidence was noted with duration of exposure and increased length of follow-up time. All but one of the cancer cases were respiratory and occurred with 6 or more months of exposure. Some other studies have been performed but they all suffer from inadequate study design or methodology. Significant increases in lung cancer incidence among rubber manufacturing plant workers were noted (Delzell and Monson, 1982). Thiess *et al.* (1980) noted an increase in lung cancer and cancer of the lymph system in acrylonitrile processing workers. Werner and Carter (1981) noted a statistically significant increase in stomach and pulmonary cancer among workers in the polymerisation of acrylonitrile and the spinning of acrylic fibers. Quast *et al.* (1980) and Maltoni *et al.* (1977) exposed Sprague-Dawley or Fischer rats, respectively, to acrylonitrile and showed statistically significant, usually dose-dependent, increases in tumours of the central nervous system (astrocytomas), Zymbal gland, stomach, tongue, small intestine and/or the mammary gland. Developmental studies showed a significant increase in offspring with malformations as well as a decrease in the litter size (Beliles *et al.*, 1980).

9. Key Risk Management Considerations:

None, since no guidelines for ambient air exist.

10. Multimedia Considerations of Guidelines:

The oral drinking water unit cancer risk for acrylonitrile is reported at 1.5×10^{-5} per ($\mu\text{g}/\text{L}$). The oral slope factor was calculated as 0.54 per ($\text{mg}/\text{kg}/\text{day}$). The ambient water quality criteria for freshwater aquatic organisms show the acute LEC to be 7,550 $\mu\text{g}/\text{L}$ and the chronic LEC to be 2,600 $\mu\text{g}/\text{L}$.

11. *Other Relevant Factors:*

The US EPA (1999) gives a medium confidence to its chronic RfC: Medium confidence in the study because only one animal species was used and no NOAEL was observed, and medium confidence in the database due to lack of chronic and sub chronic data in a second species and lack of inhalation reproductive studies when oral studies show reproductive effects.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The chronic inhalation reference exposure level for acrylonitrile is $2 \mu\text{g}/\text{m}^3$ and has been adopted from the US EPA. A unit cancer risk factor of 2.9×10^{-4} has been adopted, which is equivalent to 0.003 $\mu\text{g}/\text{m}^3$ at 1 in 10^6 excess cancer. Acrylonitrile is listed as a substance requiring the calculation of annual average concentration. Chronic exposure reference levels should be compared with modelled annual average air concentrations.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritized. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and re-submission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

Office of Environmental Health Hazard Assessment, 1988. Proposition 65 Risk Intake Levels for Acrylonitrile.

Risk Assessment Advisory Committee, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines.

Key Reference(s):

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and Development, Washington, D.C., U.S.A.

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OEHHA, 1997b. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

The guideline is current, but updates using new California risk assessment evaluations are being considered in the California Senate. Acrylonitrile is regulated under Proposition 65, Title 22, Sec. 12705b. "The cancer potency factors have been used as a basis for regulatory actions, ... and are used in a variety of risk assessment scenarios, including, but not limited to, risk assessments conducted for the Air Toxics Hot Spots Information and Assessment Program and for CERCLA/RCRA programs" (California EPA, 1994).

8. Key Risk Assessment Considerations:

California agrees with the EPA's RfC of $2 \mu\text{g}/\text{m}^3$ as its non-cancer chronic inhalation Reference Exposure Level (OEHHA, 1997b). The toxicological end-points to be considered in the determination of a hazard index are the irritation of the respiratory system and skin, or some other skin effects. Acrylonitrile is also listed as a substance whose emissions must be quantified. A risk assessment of acrylonitrile has been carried out under Proposition 65. California used the upper 95% bound on US EPA unit risk and modified this for a 70 year lifetime exposure, rather than 60 used by the US EPA. This gave an inhalation unit risk of $2.9 \times 10^{-4} \mu\text{g}/\text{m}^3$. This is equivalent to an estimated excess cancer risk of 1 in 10^6 for lifetime exposure to $0.003 \mu\text{g}/\text{m}^3$ of acrylonitrile.

9. Key Risk Management Considerations:

The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in a screening risk assessment to determine the maximum offsite cancer risk for exposed human population. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses, and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993). Acrylonitrile is not one of the substances requiring non-inhalation modelling. However, the oral unit risk for acrylonitrile is shown to be 1 mg/kg/day compared to the US EPA at 0.54 mg/kg/day, showing the US EPA's value to be 1.9-fold lower.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL; 24-hour average) for acrylonitrile is $0.4 \mu\text{g}/\text{m}^3$ and the Allowable Ambient Limit (AAL; annual average) is $0.01 \mu\text{g}/\text{m}^3$ corresponding to an excess lifetime cancer risk of 1×10^{-6} .

4. *Application:*

"... The Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Key Reference(s):

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency, Office of Research and Development, Washington, DC.

US EPA, 1983. Health Assessment Document for Acrylonitrile. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA-600/8-82-007 F. EPA

International Agency for Research on Cancer (IARC). 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 19. IARC, Lyons, France.

International Agency for Research on Cancer (IARC). 1982. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. IARC Monographs, Suppl. 4. IARC, Lyons, France.

American Conference for Governmental Industrial Hygienists (ACGIH). 1986. Documentation of the Threshold Limit Values. Fifth Edition. ACGIH, Cincinnati, Ohio.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was used. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to. However, external peer reviews on the Massachusetts methodology and guideline documentation have been carried out and public input was solicited at a minimum of two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE Staff). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each individual AAL will undergo review at least every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

Massachusetts uses occupational literature as a database for assessing acute and chronic toxicity of chemicals, and to select a beginning number for use in deriving preliminary human exposure limits for chemicals with threshold effects. The Most Appropriate Occupational Limit (MAOL) is defined as the

occupational limit which provides the best protection against the greatest number of documented health effects. The results of the scoring for acute and chronic health effects is obtained by combining the MAOL with a severity factor according to a scoring matrix. The weight-of-evidence classification for acrylonitrile, for acute and toxic effects as well as animal and human carcinogenicity, places it in Group 'A' as a human carcinogen. Using the EPA's Gene-Tox database as the source of scientifically valid data, acrylonitrile was given a score of 'A' for sufficient mutagenicity on the basis of positive results in bacterial gene mutation assays (*Salmonella typhimurium* and *E. coli*) and positive cell transformation assays (Syrian hamster embryo).

The unit risk value of 6.8×10^{-5} is adopted from the US EPA. The Allowable Ambient Limit (AAL) for acrylonitrile corresponding to an excess lifetime cancer risk of 1×10^{-6} was determined to be $0.01 \mu\text{g}/\text{m}^3$. AALs are based on both threshold and non-threshold health effects and correspond to either the Threshold effects Exposure Limit (TEL) or the Non-threshold effects Exposure Limit (NTEL), whichever is lower.

The 24 hour average concentration of $0.4 \mu\text{g}/\text{m}^3$ was based on the US EPA chronic RfC divided by 5. This assumes that 20% of exposure to acrylonitrile is from air.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population. The upper bound unit cancer risk for acrylonitrile is 6.8×10^{-5} . This has been adopted from the US EPA. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical is set at 1×10^{-6} . The Division of Air Quality Control plans to employ the AALs in the permitting, compliance, and enforcement components of the air toxics program.

10. Multimedia Considerations of Guidelines:

A multimedia exposure adjustment factor of 20% is systematically applied as a relative source contribution factor. The 1994 revision states that the method to derive AALs has not changed. When adequate cancer potency data exist, the approach of applying an uncertainty factor (NTEL) is used to develop a limit based on non-threshold effects. The AAL will then continue to be the lower of the values of the TEL or the NTEL (ORS, 1994).

11. Other Relevant Factors:

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Michigan (Department of Natural Resources)

3. *Guideline Value(s):*

The screening level (Initial Threshold Screening Level; ITSL) in Michigan is set at $2 \mu\text{g}/\text{m}^3$ using an averaging time of 24 hr.

The Initial Risk Screening Level (IRSL), based on an annual average, is $0.01 \mu\text{g}/\text{m}^3$ which is related to a cancer risk level of one in a million.

The Secondary Risk Screening Level (SRS�) is $0.1 \mu\text{g}/\text{m}^3$ which is related to a cancer risk level of 1 in 100,000.

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxics rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. Furthermore, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

Michigan Department of Natural Resources/ Environmental Quality, 1995/1997. Air Toxics Screening Levels. Air Quality Division.

Key Reference(s):

O'Berg, M. 1980. Epidemiologic Study of Workers Exposed to Acrylonitrile. J. Occup. Med. 22: 245-252.

Quast, J.F., D.J. Schuetz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980. A two-year Toxicity and Oncogenicity Study with Acrylonitrile following Inhalation Exposure of Rats. Dow Chemical Co. Toxicology Research Laboratory, Midland, MI.

US EPA, 1983. Health Assessment Document for Acrylonitrile. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA-600/8-82-007 F. EPA.

US EPA, 1999a. Integrated Risk Information System (IRIS) Database. On-line. US Environmental Protection Agency. Office of Research and Development, Washington, D.C., U.S.A.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months while a complete list of all screening levels is published at the beginning of each year.

8. *Key Risk Assessment Considerations:*

When IRSL and SRS� values are established for carcinogens, they are based on the cancer potency values published by the US EPA. If these values are not available, the EPA's HEAST values are used as the basis. If none of these are found, the toxicologist establishes the screening levels using inhalation toxicity data, if available. Michigan uses the same data as the US EPA for the determination of unit risk. The evaluation of the same studies that the US EPA used for its determination of cancer risk (O'Berg, 1980; Quast et al., 1980) were determined to be sufficiently robust (sufficiently large cohort, adjustment for smoking in humans; 2-year rat inhalation and oral studies) for use by Michigan. Acrylonitrile is classified by weight-of-evidence as a probable human carcinogen (B1) in accordance with the US EPA. The unit risk of 6.8×10^{-5} per $\mu\text{g}/\text{m}^3$ was calculated from a relative risk model adjusted for smoking and based on a continuous lifetime equivalent of occupational exposure (Section 11.1).

The US EPA RfC of $2 \mu\text{g}/\text{m}^3$ was adopted for the ITSL. See Section 11.1.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No Information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* New Jersey

3. *Guideline Value(s):*

The reference concentration for inhalation of acrylonitrile in New Jersey is $2 \mu\text{g}/\text{m}^3$.

The unit risk factor for inhalation of acrylonitrile is 6.8×10^{-5} .

4. *Application:*

The list of reference concentrations for inhalation are maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consist of two levels. The first risk screening level uses information from permit applications and generalised worst case assumptions to estimate non-cancer and cancer risk from inhalation. Sources which fail the first level screening are submitted to a second risk screening level which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources which fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.).

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The risk screening procedure considers only inhalation exposure. Every source is not modelled individually. Instead, monographs, developed using dispersion models, are used to calculate ambient air concentrations of each source chemical. New Jersey adopted the US EPA RfC (see 7.1). The RfC is to be compared to the maximum annual average ambient air concentration.

In the case of carcinogens, the averaging time is annual assuming ambient exposure levels to the chemical all the time. Long term effects are calculated on the basis of the maximum annual average air concentration. In the case of carcinogens, this latter concentration is multiplied by the unit risk factor to obtain the incremental risk for a chemical. In addition, New Jersey believes that just because a chemical has not shown carcinogenicity, it is not a proven non-carcinogen. The Air Quality Permitting Program (AQPP) assumes a linear dose-response relationship, with no threshold, for carcinogenic substances. The compound is classified as a B1 carcinogen according to the US EPA classification of carcinogenicity. New Jersey adopted the US EPA unit risk factor of 6.8×10^{-5} .

9. Key Risk Management Considerations:

Public health risk estimates of incremental risk for inhalation of carcinogens are calculated as a product of the maximum annual average ambient air concentration of a chemical ($\mu\text{g}/\text{m}^3$) and the chemical-specific unit risk factor ($\mu\text{g}/\text{m}^3$)⁻¹. The AQPP uses this information for its risk management. The policy has the following three guidelines: (1) if the incremental cancer risk is less than 1 in 10^{-6} , the risk is considered negligible, (2) if the risk is greater than 1 in 10^{-4} , the risk is considered unacceptable, and (3) if the risk lies between the preceding two values, the risk is evaluated on a case-by-case basis.

10. Multimedia Considerations of Guidelines:

The risk screening procedure considers only exposure by the inhalation route.

11. Other Relevant Factors:

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC; 1-h average air concentration) is $220 \mu\text{g}/\text{m}^3$ and the Annual-average-based Guideline Concentration (AGC) is $0.01 \mu\text{g}/\text{m}^3$. Acrylonitrile is classified as a high toxicity air contaminant and is given an "A" 6NYCRR Part 212 Environmental Rating. For compounds with such a rating, the maximum annual average ambient impact is required not to exceed the AGC. Similarly, the one hour short-term SGC must also not be exceeded. "A" rated compounds also require the application of "Best Available Control Technology" (BACT) to achieve 99% or greater pollution control.

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

Key Reference(s):

United States Environmental Protection Agency (US EPA). 1986. Guidelines for Carcinogen Risk Assessment. Federal Register 51: 33992-34003. (9/24/86)

American Conference of Governmental Industrial Hygienists, 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

6. Peer Review Process and Public Consultation:

The scientific documents prepared by the New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guidelines development process.

7. Status of Guideline:

Current. The New York State Air Guide - 1 is dated 1991. The latest version of the companion Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

8. Key Risk Assessment Considerations:

Acrylonitrile is classified as a high toxicity air contaminant by New York State (1994). This classification includes human carcinogens, potential human carcinogens and other substances posing a significant risk to humans. Classification is based on data from epidemiology studies, the full range of toxicology studies in animals, and a review of the scientific and medical literature. Data from inhalation studies takes precedence over data from studies using other routes of exposure. Particular attention is paid to information on carcinogenic or genotoxic potential. Models using low-dose linearity are preferred unless there is sufficient evidence to support another dose-response extrapolation model. The derivation of the AGC is based on studies with data that show biologically and statistically significant tumour type incidence, duration and route of exposure, as well as, the greatest sensitivity. In the absence of appropriate scientific data the dose extrapolation from animal to human is performed by surface area conversion. New York adopted the US EPA cancer unit risk for its AGC.

New York derived a Short-term Guideline Concentration (SGC; 1 hr) by applying an uncertainty factor to the NIOSH REL-TWA of 1 ppm (2,170 $\mu\text{g}/\text{m}^3$).

9. Key Risk Management Considerations:

Environmental Ratings are reviewed for each contaminant every time a Certificate to Operate comes up for renewal. A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses to be employed in the permitting process.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

NIOSH (1988,1997) notes that since acrylonitrile is a potential carcinogen, the REL-TWA of 1 ppm (2,170 $\mu\text{g}/\text{m}^3$) is based on the lowest feasible concentration.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

The unit cancer risk for a lifetime exposure to $1 \mu\text{g}/\text{m}^3$ of acrylonitrile is determined to be 2×10^{-5} for lung tumours. Acrylonitrile is classified as an IARC Group 2A carcinogen because it is carcinogenic to animals with limited evidence of carcinogenicity in humans.

4. *Application:*

The WHO Air Quality Guidelines are intended to provide a basis to protect public health from adverse effects of air pollution, and to provide background information and guidance to governments in making risk management decisions. However, it should be noted that no standards as such are promulgated by the WHO.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426p.

Key Reference(s):

Delzell, E. and R.R. Monson. 1982. Mortality among Rubber Workers. VI. Men with Exposure to Acrylonitrile. *J. Occup. Med.* 24: 767-769.

Maltoni, C., A. Ciliberti and V. diMaio. 1977. Carcinogenicity Bioassays on Rats of Acrylonitrile Administered by Inhalation and by Ingestion. *Med. Lavoro.* 68: 401-411.

O'Berg, M. 1980. Epidemiologic Study of Workers Exposed to Acrylonitrile. *J. Occup. Med.* 22: 245-252.

Quast, J.F., D.J. Scheutz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980. A Two-Year Toxicity and Oncogenicity Study with Acrylonitrile Following Inhalation Exposure of Rats. Prepared by the Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical USA, Midland, MI, for the Chemical Manufacturers Association, Washington, DC.

US EPA. 1983. Health Assessment Document for Acrylonitrile. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC.

Werner, J.B. and J.T. Carter. 1981. Mortality of United Kingdom Acrylonitrile Polymerisation Workers. *Br. J. Ind. Med.* 38: 247-253.

World Health Organization. 1983. Acrylonitrile. *Environmental Health Criteria*, No. 28.

6. Peer Review Process and Public Consultation:

Scientific background documents were prepared by experts and submitted to working groups consisting of international experts to provide a basis for discussion. After a series of meetings and internal and external reviews by experts and representatives of the Member States of the Region, the resultant conclusions and recommendations were presented at a final meeting where they were adopted by consensus of the representatives. In addition, peer-reviewed scientific research data were employed in the development of these documents.

7. Status of Guideline:

Currently applicable.

8. Key Risk Assessment Considerations:

Acrylonitrile showed evidence of mutagenicity in *Salmonella typhimurium*, *Escherichia coli* and *Saccharomyces*. There was also evidence of cell transformation of Syrian hamster embryo cells, sister chromatid exchange in Chinese hamster embryo cells, as well as, in human lymphocytes in the presence of an activation system, and chromosomal aberrations in hamster lung fibroblasts. *In vivo* short-term studies were predominantly negative. Long-term carcinogenicity bioassays in rats showed an increased occurrence of tumours of the central nervous system, Zymbal gland, stomach, tongue, mammary glands and small intestine in both males and females. These results are considered to show sufficient evidence of carcinogenicity in rats.

In humans, both the toxicological and carcinogenic effects of acrylonitrile were examined. The toxicological effects of acrylonitrile were demonstrated by irritation of the eyes, nose and throat, dull headaches, fullness of the chest, itching and nervous irritability. At higher concentrations, vertigo, nausea, vomiting, tremors, convulsions, diarrhoea and jaundice were sometimes noted. Of the twelve epidemiology studies reviewed, only five showed evidence of cancer risk. The studies had some deficiencies in methodology and consideration of major factors in the analysis. On the basis of the results found in these studies, it was concluded that there was limited evidence of carcinogenicity in humans.

The epidemiological study of O'Berg (1980) presents the clearest available evidence of acrylonitrile being a lung carcinogen in humans. 43 cases of lung cancer were reported as opposed to 37.1 expected. The follow-up study (O'Berg, 1985), gave a lower relative risk (R) of 10 (expected)/7.2(observed). Using the assumption of the US EPA (1983) the average lifetime exposure

(X) was calculated as $930 \mu\text{g}/\text{m}^3$. Using the average relative risk model, the unit lifetime risk (UR) for exposure to $1 \mu\text{g}/\text{m}^3$ can be calculated as 1.7×10^{-5} [$\text{UR} = P_0(R-1)/X = 0.04(1.4-1)/930$]. This is similar to the estimated risk of 1.5×10^{-5} derived rat studies by the US EPA (1983).

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

Exposure from air, drinking water and food was considered in the evaluation of acrylonitrile. However, this did not contribute to the determination of the IARC classification or the determination of unit risk.

11. Other Relevant Factors:

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* The Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

The national air limit value not to be exceeded for acrylonitrile is $1 \mu\text{g}/\text{m}^3$ for an annual average with a target value of $0.1 \mu\text{g}/\text{m}^3$. The emission standard is $5000 \mu\text{g}/\text{m}^3$ for a mass flow of 5.0 kg per hour or more. Acrylonitrile is classified as C.3, a non-threshold carcinogen. This classification is defined by the emission concentration of $0.1 \mu\text{g}/\text{m}^3$ which results in an additional cancer risk of 1 in 10^6 with lifetime exposure. This compound is black listed in air, therefore, the target is to have zero release.

Note: Acrylonitrile is erroneously classified as C.2 in Appendix 4 of The Netherlands Emission Regulations. All other data in all the available documentation are consistent with the C.3 classification in Chapter 2.

4. *Application:*

Limit values are non-statutory environmental quality objectives that are considered policy guidelines which should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effect-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effect-oriented guidelines.

The target value is the level at which the risk of adverse effects to the ecosystem, functional properties of the environment or other compartments are considered negligible. The ultimate objective of the environmental quality guidelines of The Netherlands is that the target value might eventually become similar to the limit value.

5. *Documentation Available:*

The Netherlands MHSPE, 1994. Environmental Quality Objectives in The Netherlands. A review of environmental quality objectives and their policy framework in The Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

NeR Staff Office, 1992. The Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 pp. + Appendices.

Van de Plassche, E.J. and G.J.M. Bockting. 1993. Towards Integrated Environmental Quality Objectives for Several Volatile compounds. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Report no. 679101 011.

Key Reference(s):

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances, but are only available in Dutch.

6. Peer Review Process and Public Consultation:

No specific information on this issue was presented in the available English documentation.

7. Status of Guideline:

Current. In 1993, recent studies were evaluated and the determination was made that no updating of the information for acrylonitrile was required.

8. Key Risk Assessment Considerations:

Acrylonitrile is considered to be a carcinogen, class C.3, under The Netherlands Emission Regulations on the basis of the Minimum Immission Concentration at which a risk of one extra cancer case occurs per 10^6 given lifelong exposure. The national guidelines issued are derived from occupational hygiene limit values (Maximum Acceptable Concentration, or MAC values) dating from 1992. The national limit values for air are based on extensive risk assessment. The annual average Maximum Acceptable Concentration is $9,000 \mu\text{g}/\text{m}^3$ which is a value used as an environmental hygiene criterion for the workplace. The Maximum Permissible Concentration (MPC) of acrylonitrile in air is $10 \mu\text{g}/\text{m}^3$. No ambient air concentrations were available.

9. Key Risk Management Considerations:

Risk management is carried out by progressive criteria setting. In principle, the target value is set to the negligible concentration or the naturally occurring background value, whichever is higher. A limit value should not be exceeded and a guidance value should be avoided whenever possible. With time, the values are tightened to reach the target value.

Carcinogens without a threshold value are subject to compulsory minimisation under The Netherlands Emission Regulations. Acrylonitrile is black-listed for emission into air in The Netherlands. Substances are placed on this list on the basis of their environmentally harmful properties and not on the risk estimate of the substance. Furthermore, the black list is only relevant to source-oriented policy. The best available means (bam) has to be used to reduce pollution by this substance. Since these substances may occur naturally or may be produced from other countries, the substance(s) may be included on a priority substance list for special attention.

10. *Multimedia Considerations of Guidelines:*

Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. Information is currently available on the MPC and the NC (negligible concentration) of water, soil, sediment and air.

11. *Other Relevant Factors:*

No information

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Swedish Environmental Protection Agency

3. *Guideline Value(s):*

No guidelines.

4. *Application:*

No information.

5. *Documentation Available:*

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. *Chemosphere* 27: 1691-1706.

Victorin, K., 1997. Personal communication.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Acrylonitrile

2. *Agency:* Environment Canada

3. *Guideline Value(s):*

Acrylonitrile has been assessed under the second Priority Substance List (PSL2). No specific air quality guideline value has been identified for acrylonitrile. However, cancer risk-based tumourigenic concentrations at 5% increase in incidence (TC₀₅) of 6 mg/m³ and 8.6 mg/m³ based on tumours observed in female and male rats, respectively, have been proposed for acrylonitrile.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines. Based on the draft document released in July 1999, it is proposed that acrylonitrile be considered "toxic" as defined in Section 11 of CEPA..

5. *Documentation Available:*

Environment Canada, 1999. *Canadian Environmental Protection Act* Priority Substances List Assessment Report (draft) - Acrylonitrile, Environment Canada, Health Canada. Minister of Supply and Services Canada; Ottawa, Canada. February 1999.

Environment Canada, 1999. *Canadian Environmental Protection Act* Priority Substances List Assessment Report (draft) - Acrylonitrile, Supporting Documentation, Health-related Sections (Exposure), Environment Canada, Health Canada. Minister of Supply and Services Canada; Ottawa, Canada. March 1999.

Environment Canada, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA), Environment Canada, PSL2 Secretariat. October 1995. Also available on the Internet:
www.ec.gc.ca/cceb1/eng/policy_e.htm

Key Reference(s):

Quast, J.F., D.J. Scheutz, M.F. Balmer, T.S. Gushow, C.N. Park and M.J. McKenna. 1980a. A Two-Year Toxicity and Oncogenicity Study with Acrylonitrile Following Inhalation Exposure of Rats. Prepared by the Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical USA, Midland, MI, for the Chemical Manufacturers Association, Washington, DC.

6. Peer Review Process and Public Consultation:

CEPA underwent comprehensive public consultation and review. The PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released. Experts from various fields are invited by Environment Canada to participate actively in the assessment process. They form an Environmental Resource Group, which can include scientific and technical experts from all levels of government, industry, academia, environmental groups, and other interested parties. Acrylonitrile assessment report has been released in July 1999 for public review.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

The inhalation study of Quast *et al.* (1980a) has been chosen as the key source for quantitative data and astrocytoma of the CNS has been considered the most appropriate tumour type for cancer risk estimation (see also Section 3.5). This study was selected because of the size of the groups ($n=100$) and it was a lifetime study (two years of exposure), despite the fact that there were only two doses tested. Both benign and malignant tumours of the astrocytoma type in the CNS were combined for the calculation, using a multistage model (GLOBAL 82). Tumour incidences have been adjusted to exclude animals dying before six months (prior to observation on the first tumour). Dose scaling between animals and humans was considered to account for differences in inhalation volume and body weight, based on the averaged breathing volume of $0.11 \text{ m}^3 \text{ air/day}$ for a 0.35 kg rat and $23 \text{ m}^3/\text{day}$ for a 70 kg adult human.

The tumourigenic concentration at 5% increase in incidence or mortality (TC_{05}) for the combined tumour incidence of tumour in the brain and the spinal cord in female rats is estimated to be $6000 \mu\text{g}/\text{m}^3$ ($8900 \mu\text{g}/\text{m}^3$ for the male rats). This is the lowest TC_{05} (human equivalent value). The lower 95% confidence limit is $4500 \mu\text{g}/\text{m}^3$. The application of a margin of safety factor of 5000 and 50000 to the TC_{05} will provide protection to that associated with the range for low dose risk estimates generally considered by various agencies to be "essentially negligible", i.e. 10^{-5} and 10^{-6} respectively (Health Canada, 1996). Thus, at an exposure concentration of $1.2 \mu\text{g}/\text{m}^3$ for a lifetime, the likelihood of tumour incidence is at one in a hundred thousand. This value is in close agreement with the risk specific concentration at an equivalent risk level based on the ED_{10} for female rats as estimated by TERA.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or <i>Ontario Ministry of Environment and Energy</i>
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either Reference Exposure Level</i> as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or <i>Recommended Exposure Limit</i> used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumourigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumourigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
AMMONIA**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air quality standards will be reviewed over the next several years. Ammonia was identified as a priority for review based on both its pattern of use in Ontario, and toxicological information that has been published subsequent to the development of the existing standard in 1970. A review of scientific and technical information relevant to setting an air quality standard for ammonia has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour point of impingement (POI) standard for ammonia.

Ammonia is a naturally occurring, colourless, acrid-smelling gas. It is widely used in a variety of manufacturing processes, but is mostly used as a fertilizer. Much of the ammonia in air results from the decomposition of organic matter and other biological activities. Among the chemicals listed in the National Pollutant Release Inventory of Canada, ammonia is one of the five highest released substances in air in Ontario since the reporting year of 1993. Ambient concentrations of ammonia measured by the Ministry of the Environment downwind from a foundry in 1989 were below the detection limit of $1 \mu\text{g}/\text{m}^3$. A value of $0.6 \mu\text{g}/\text{m}^3$ has been reported as a background concentration in southern United States.

Ammonia vapour is an irritant to the eyes and the respiratory tract. Damage to the bronchial epithelium and the alveolar membrane have been documented at high concentrations while severe acute over-exposure can lead to death within minutes. Ammonia in high concentrations (liquid or gas) will kill most organisms. Nonetheless, since it is readily diluted and degraded in air, it does not stay airborne for more than a week. Ammonia from accidental spills or emissions does not persist in the environment. However, elevated ammonia concentrations over a long period of time may occur where there are intensive manure applications and animal farming activities, and which may eventually be detrimental to the environment.

Ontario currently has a 24-hour average ambient air criterion (AAQC) of $3,600 \mu\text{g}/\text{m}^3$ and a half-hour Point of Impingement (POI) standard of $3,600 \mu\text{g}/\text{m}^3$ for ammonia. These criteria have been established on the basis of odour effects.

In revising the air quality standards of Ontario, the Ministry of the Environment is reviewing and considering risk assessments, and standards and guidelines, used by environmental agencies worldwide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan and, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of

Environmental Medicine and the Canadian Federal Government. All of the agencies examined considered the irritant effects of ammonia as the predominant adverse effect of this substance. Most of the U.S. states have adopted the inhalation Reference Concentration (RfC) of $100 \mu\text{g}/\text{m}^3$ developed by the US EPA for their long-term guidelines. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the Reference Concentration established by the US EPA. After reviewing additional toxicological information, the Ministry considers the uncertainty factors used by the US EPA to derive its RfC reasonable. Therefore, a 24-hour AAQC of $100 \mu\text{g}/\text{m}^3$ based on the RfC is proposed.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for ammonia:

- **a 24-hour average AAQC of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ammonia based on the adverse health effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $300 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $3600 \mu\text{g}/\text{m}^3$ to this revised level of $300 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$300 \mu\text{g}/\text{m}^3$ to $3,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ammonia.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
- For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Ammonia was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information that has been published subsequent to the development of the existing standards in 1970. A review of scientific and technical information relevant to setting air quality standards for ammonia has been provided in a previous document for stakeholder comments. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for ammonia.

2.0 General Information

2.1 Physical/chemical Properties

The following list provides some general information on ammonia and its properties:

CAS #	7664-41-7
RTECS #	BO0875000; (BQ9625000 in aqueous solution)
UN #	UN1005 (air); UN2073 >40% solu.; UN2672 >55% solu.)
Conversion Factors	1 ppm = 0.708 mg/m ³ @ 20 °C and 760 mm Hg 1 mg/m ³ = 1.412 ppm @ 20 °C and 760 mm Hg
Boiling Point	-33.35 °C @ 1 atm.
Melting Point	-77.74 °C @ 1 atm
Henry's Law Constant	Range of Pa m ³ /mol
Log K _{ow}	not available
Formula	NH ₃
Molecular Weight	17.03 g/mol
Vapour Density (air = 1)	0.6
Vapour Pressure	6441 mmHg @ 20 °C
Common Synonyms	ammonia, anhydrous; nitro-sil

Ammonia (NH₃) is a colourless gas at ambient temperature. Its odour is characterized as sharp, pungent and intensely irritating. The reported odour threshold values range from 0.03 to 37.5 mg/m³ (0.043 to 53 ppm) with a geometric mean is 11.8 mg/m³ (17 ppm) (AIHA, 1989; Cheminfo, 1996; Devos *et al.*, 1990; Ruth, 1986; Verschueren, 1983; WHO, 1986). The concentration at which ammonia becomes irritating is estimated to be above 50 mg/m³ (WHO, 1990).

2.2 Uses

Ammonia is a naturally occurring substance. It is also one of the most extensively used industrial chemicals (WHO 1990). Ammonia is mostly used in the production of fertilizers, nitrogen-containing organic compounds, refrigerants, synthetic fibres, explosives, food additives, and as cleaning and descaling agents. The total annual commercial production of ammonia was estimated to represent approximately 1-5% of global natural ammonia formation (ATSDR, 1990).

2.3 Sources and Levels

Ammonia is ubiquitous and is present in the environment as a result of natural biological processes and industrial activities. About 99% of ammonia present in the atmosphere is released by the breakdown of organic waste matter (WHO, 1986). Therefore, any natural or industrial process that concentrates nitrogen-containing organic matter, and makes it available for decomposition, becomes a potential source of high local concentration of ammonia. Other environmental sources include emission of industrially produced ammonia, release through agricultural fertilization, as well as coal gasification or liquefaction (WHO, 1986).

Ammonia is among the pollutants reported in the National Pollutant Release Inventory in Canada. In Canada, atmospheric releases have been consistent in the reporting years between 1993 - 1997 at about 18000 tonnes (NPRI, 1993, 1994, 1995, 1996 & 1997). Atmospheric releases in Ontario followed a similar pattern ranging from 4074 to 5340 tonnes from 1993 to 1997. During these years, ammonia was among the five highest emitted substances in Ontario. Over 60% of the total Ontario atmospheric emissions were contributed by only two facilities in Ontario, according to the 1997 report. The vast majority of these releases came from the chemical and chemical products industries, particularly in the making of fertilizers. Fertilizer production accounted for around 80% of total air emissions. Other industrial point sources include primary metal industries, textile product industries, food industries, industries that produce paper and allied products, non-metallic mineral products, industrial and heavy (engineering) construction industries, as well as other utility industries.

From an examination of recent applications for Certificates of Approval in Ontario, a sample of 61 Certificates covering emissions of ammonia to the atmosphere, were identified. The median Ground Level Concentration (GLC), predicted by Regulation 346 modelling, was approximately $12.9 \mu\text{g}/\text{m}^3$. The maximum and minimum GLC predicted were $3,561.8 \mu\text{g}/\text{m}^3$ and $0.00001 \mu\text{g}/\text{m}^3$, respectively.

2.4 Ambient and Indoor Air Concentrations

An airborne concentration of $0.6 \mu\text{g}/\text{m}^3$ (0.9 ppb) has been reported as a possible background level in the southern United States (ATSDR, 1990), although the typical levels of ammonia in urban and non-urban sites are in the order of 20 and $5 \mu\text{g}/\text{m}^3$, respectively (WHO, 1986). Nevertheless, it has been noted that the general ambient atmospheric levels are of no concern with respect to discomfort or acute toxicity (WHO, 1986).

In non-urban areas, the most common source of ammonia is the use of fertilizers. Ambient half-hour concentrations of ammonia, measured downwind from a foundry in 1989, were below the detection limit of $1 \mu\text{g}/\text{m}^3$ (MOEE, 1997). However, high concentrations over a long period of time may occur where there are intensive animal farming activities. For example, concentrations as high as $1,540 \mu\text{g}/\text{m}^3$

have been reported over cattle feed lots (ATSDR, 1990; WHO, 1986), while indoor air concentrations can reach up to 35,000 $\mu\text{g}/\text{m}^3$ (50 ppm) in swine or poultry confinement buildings. The WHO (1986) reported ammonia concentrations ranging from 4,200 to 24,500 $\mu\text{g}/\text{m}^3$ (6 - 35 ppm) in swine raising facilities. In a study involving 108 farms and 207 swine producers in the U.S. (Eastern Iowa), the indoor air ammonia level in these facilities averaged 3,700 - 4,700 $\mu\text{g}/\text{m}^3$ (geometric means) (Donham *et al.*, 1995). Industrial air levels at fertilizer production plants may reach values up to 53,000 $\mu\text{g}/\text{m}^3$ (75 ppm; ATSDR, 1990).

2.5 Environmental Fate

The environmental fate of ammonia has been reviewed by the US EPA (1989) and WHO (1986). Ammonia is central to the environmental cycling of nitrogen. Even before contribution from human sources, a network of active and efficient, natural organic and inorganic processes, that trap, transform, produce or use ammonia have already existed. Because the nitrogen cycle is dynamic, no dramatic build up of ammonia is expected to occur as a result of the additional inputs from human sources.

In the atmosphere, ammonia may undergo many transformations, and is expected to have a short residence time of 5 to 10 days. The most important removal mechanism is dissolution in water droplets, which are subsequently be removed by rain or washout. Ammonia can also be removed by reaction with OH radicals. In soil, the most likely fate of ammonia is conversion to nitrates through the nitrification action of microorganisms. Nitrates are in turn lost from soils by leaching, denitrification and uptake by the plant root systems. In natural water, ammonia can be removed by bacteria through nitrification, assimilation by aquatic algae and macrophytes, adsorption on particulates and subsequent sedimentation, and volatilization. These processes contribute to the natural cycling of nitrogen in the environment, and help to prevent the persistence and accumulation of elevated levels of ammonia.

3.0 Toxicology of Ammonia

The following toxicological review of ammonia is primarily focusses on inhalation exposure, since this is the primary route of exposure from atmospheric emissions. Data on other exposure media are included where relevant or where inhalation data is lacking.

Ammonia is an essential chemical to animals and humans. In the human body, it is produced from nitrogen containing substances such as proteins and acidic bases. More than 50 mg of ammonia per human body weight is produced endogenously for the maintenance of acid/base balance and nitrogen metabolism (ATSDR, 1990).

In short-term exposures (up to 2 min.) with volunteers, 83 - 92% of the inhaled ammonia (57 - 500 ppm or 40 - 354 mg/m³) was retained in the nasal mucosa. Longer-term exposures (10 - 27 min.) to a high concentration (500 ppm or 354 mg/m³), resulted in decreased nasal retention and increased expired concentrations (350 - 400 ppm or 248 - 283 mg/m³). The occurrence of nasal and pharyngeal irritation, but no tracheal irritation, suggested that ammonia was retained in the upper respiratory tract (ATSDR, 1990)

3.1 Acute Toxicity

Ammonia is corrosive and irritating, and can cause severe skin and eye burns in humans. Clinical effects of ammonia exposure are manifested as irritation to the eye, skin, nose, mouth, throat or the lungs. General symptoms of ammonia exposure may range from wheezing, coughing, nasal discharges, bronchial discharges, upper airway obstruction, bronchospasm to lung edema (WHO, 1986; US EPA, 1989). The respiratory symptoms are usually reversible (WHO, 1986). The severity of effects depends on the level of exposure. Throat irritation was observed when exposed to ammonia at 280 mg/m³ and cough resulted at 1200 mg/m³. In addition, 1700 mg/m³ of ammonia was life-threatening and above 3500 mg/m³ death may occur (WHO, 1986).

Seven volunteers were exposed to ammonia at 500 ppm (355 mg/m³) for 30 min. using an oral-nasal mask (Silverman *et al.*, 1949 as cited in OEHHA, 1998). Although the reported symptoms varied widely, upper respiratory irritation was reported for all test subjects. Irritation was graded as severe in two volunteers, and only two subjects were able to continue nasal breathing throughout the 30 minute exposure. Responses included irritations of the nose and throat, hypoesthesia of the exposed skin, and tearing of the eyes. In two subjects, the nasal-pharyngeal irritation persisted for 24 hours following the exposure.

In another human study, 8 subjects with previous exposures, and 8 subjects with no previous exposures (naive group), were exposed to ammonia for two hours at concentrations of 50, 80, 110 and 140 ppm (36, 57, 78 and 99 mg/m³), respectively (Verberk, 1977 as cited in OEHHA, 1998). The group with no previous exposures could not tolerate the 99 mg/m³ concentration for two hours, and had several complaints during exposure to 78 mg/m³ for one hour. None of the volunteers demonstrated a decrease in measured pulmonary function tests, including the vital capacity, forced expiratory volume (1 second) and the forced inspiratory volume (1 second) following ammonia exposure. The results showed a greater sensitivity to ammonia for the naive group in smell, eye irritation, cough, general discomfort, headache and irritation of the chest. After 30-minutes of exposure at 36 mg/m³, eye, nose or throat irritation, or cough urge were reported by 7 of 16 (44%) subjects. At the highest dose tested (99 mg/m³), 15 of 16 (94%) subjects reported irritation of the eyes, nose or throat or the urge to cough.

In a study by MacEwen *et al.* (1970, as cited in OEHHA, 1998) volunteers exposed to ammonia at a concentration of 36 mg/m³ (50 ppm) for 10 minutes reported moderate irritation. In the same experiment, subjects exposed to 21 mg/m³ (30 ppm) reported no increase in symptoms indicative of irritation.

In a separate experiment, ten test human subjects were exposed to ammonia at 32, 50, 72 and 134 ppm (23, 36, 51 and 95 mg/m³), respectively (Industrial Bio-Test Laboratories, 1973 as cited in OEHHA, 1998). Irritation was reported as any annoyance of the eyes, nose, mouth, throat or chest which persisted throughout the 5-minute exposure period. At a concentration of 51 mg/m³, three subjects reported eye irritation, two had nasal irritation and three had throat irritation. At 95 mg/m³, five of the ten subjects experienced irritation and tearing of the eyes, seven complained of nasal irritation and eight had throat irritation while one complained of chest irritation.

Animal studies generally support the irritative and corrosive properties of inhaled ammonia (US EPA, 1997). The LC₅₀ (median lethal concentration) for rats has been reported to range from 31612 mg/m³ for a 10-min. exposure, to 11620 mg/m³ for a 60-min. exposure (WHO, 1986). In albino mice, the 1-hr LC₅₀ has been estimated at 3,000 mg/m³ (Calabrese and Kenyon, 1991).

3.2 Subchronic/Chronic Toxicity - Inhalation

Chronic exposure to 28 mg/m³ ammonia vapour has been reported to result in headaches, nausea and reduced appetite (US EPA, 1989). The effects of long-term exposure to ammonia involving workers of a soda ash plant has been studied by Holness *et al.*, (1989 as cited in US EPA, 1998). Fifty-two exposed production workers and 31 unexposed control workers were examined. The mean age of the workers was 38.9 years, and the duration of exposure was 12.2 years. The mean time-weighted average concentrations of an 8-hour shift, for the exposed and control workers (based on data obtained from personal sampling), were 6.4 mg/m³ (9.2 ppm) and 0.21 mg/m³ (0.3 ppm), respectively. Differences in eye, skin, respiratory symptoms and lung functions were evaluated using the actual values, and with age, height and cigarettes smoked in pack-years as covariates. Although there was no statistically significant difference in the prevalence of any of the symptoms reported, plant workers exposed to ammonia reported throat discomfort, coughing, wheezing and nasal complaints, as well as skin and eye irritation. Exposed workers showed no evident changes in lung functions (reflective of effects on the lower respiratory system) when compared with controls.

In an animal study, exposure to ammonia increases the susceptibility and the severity of infection. Rat studies involving challenges with *Mycoplasma pulmonis* concomitant with exposure to ammonia indicated that the severity of rhinitis, otitis media (inflammation of the middle ears) and pneumonia, characteristic of *M. pulmonis* were increased in comparison to animals not exposed to ammonia (Broderson *et al.*, 1976 as cited in US EPA, 1998). In a separate study, a group of 295 F344 rats

were inoculated with *M. pulmonis* and exposed to either trace or 100 ppm (human equivalent concentration of 7.4 mg/m³) ammonia (Schoeb *et al.*, 1982 as cited in US EPA, 1998). Growth of *M. pulmonis* was greater in exposed animals than in controls.

3.3 Developmental/reproductive Toxicity

No information was located (ATSDR, 1990)

3.4 Genotoxicity

No information was located (ATSDR, 1990)

3.5 Carcinogenicity

Ammonia did not cause tumours, or increase the spontaneous incidence of tumours in life-time, mice studies (WHO, 1986). There was one case of a male subject who developed epidermal carcinoma of the nasal septum six months following a severe burn by accidental contact with a refrigeration ammonia-oil mixture (Shimkin *et al.*, 1954 as cited in ATSDR, 1990). However, no causal relationship between this type of tumour and ammonia exposure has been identified (ATSDR, 1990).

3.6 Environmental Effects

Studies describing the toxicological effects of ammonia on wildlife are limited, as atmospheric ammonia is not usually harmful to animals. However, ammonia can reach toxic concentrations during transport accidents near forests or remote areas. Another scenario resulting in high ammonia concentrations is the extermination of birds and mice from barns. Seven (7) minute exposures of 1,600 mg/m³ ammonia, within an enclosed building, resulted in the death of the starlings, pigeons and mice residing within the building (Environment Canada, 1984). No-observed-adverse-effects were noted in bats at concentrations of 59.8 to 1,302 mg/m³ (Environment Canada, 1984). Bats have developed a high tolerance for ammonia, as bat colonies produce an ammonia precursor, guano, which is decomposed by bacteria to produce ammonia, resulting in high atmospheric ammonia concentrations (WHO, 1986).

Ammonia is corrosive and readily soluble in water. It has been suggested that non-ionized ammonia (NH₃) is the primary toxic species to fish. However, the toxicity of ammonia in water is also dependent on the conditions of water, including, the pH, temperature, dissolved oxygen and the ionic composition of the background water (WHO, 1986). Aquatic animals generally have a low capacity to detoxify ammonia. Based on a summary of 71 toxicity tests, and 96-hour LC₅₀ values, toxicity for rainbow trout exposure to ammonia ranged from 0.16 to 1.1 mg/L (WHO, 1986). Rainbow trout appears to be the

species most sensitive to aqueous ammonia exposure (National Research Council, 1979 as cited in Environment Canada, 1984).

Ammonia may affect vegetation directly by acting on the function and structure of plants, or indirectly by changing the conditions of soil following deposition (WHO, 1986). Ammonia is a basic nutrient to, and a structural component of plants. However, depending on the sensitivities of plant species, exposure to ammonia may be deleterious to plants. Some studies conducted in The Netherlands indicated that several vegetables and trees showed signs of leaf damage by necrosis, growth reduction and increased frost sensitivity at atmospheric ammonia levels of $75 \mu\text{g}/\text{m}^3$ (annual average), $600 \mu\text{g}/\text{m}^3$ (24-hour exposure) and $10,000 \mu\text{g}/\text{m}^3$ (1-hour exposure) (Van der Eerden, 1982 as cited in WHO, 1986). An investigation of 12 accidental releases of ammonia in Southern Ontario provides relative susceptibility information of plant species to ammonia (Temple et al, 1979). The most susceptible plant species were found to be balsam poplars (*Populus balsamifera* L.), red mulberry (*Morus rubra* L.), hawthorn (*Crateagus* species) and butternut (*Juglans cinerea* L.). Conifers did not demonstrate toxic effects as the result of ammonia exposure and Maple (*Acer*) species were resistant to ammonia gas exposure (Temple et al, 1979).

4.0 Review of Existing Air Quality Regulations

4.1 Overview

The 24-hour ambient air quality criterion for ammonia in Ontario is $3,600 \mu\text{g}/\text{m}^3$ (MOEE, 1994a). The half-hour POI standard is also $3,600 \mu\text{g}/\text{m}^3$. Both were established based on the odour nuisance of ammonia.

In revising the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments, and standards and guidelines, used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency-specific summaries of information concerning air quality guidelines for ammonia are presented in Section 11.0, the Appendices of this report. Table 1 is a brief summary of the information.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria, based on 24-hour average concentrations. These factors are derived from empirical measurements and are

selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Upon examining the available air quality criteria from the various agencies (see Table 1), the adverse effects of ammonia on the upper respiratory system is the relevant end-point for establishing exposure limits. The Inhalation Reference Concentration (RfC) of $100 \mu\text{g}/\text{m}^3$ for chronic exposure, from the US EPA, has predominantly been used as the benchmark by several state agencies to derive their air quality guidelines based on a 24-hour or an annual averaging time. These include the state agencies of California, Massachusetts, Michigan and New Jersey. The air guidelines of New York State were derived from occupational exposure limits. The Netherlands derived its national air limit of $120 \mu\text{g}/\text{m}^3$ directly from its occupational hygiene limit value of $18,000 \mu\text{g}/\text{m}^3$.

California and New York have developed short-term (1-hour) air guidelines in addition to their annual criteria. The State of California derived its acute reference value of $2,100 \mu\text{g}/\text{m}^3$ based on dose response data for human respiratory irritation, using the Defined Practical Threshold methodology proposed by Lewis and Alexeeff (1989). Recently, the California Environmental Protection Agency (Office of Environmental Health Hazard Assessment) proposed a revised acute Reference Exposure Level of $3,200 \mu\text{g}/\text{m}^3$ based on the eye and respiratory irritations on humans. The State of New York derived its one-hour short-term guideline concentration of $4,000 \mu\text{g}/\text{m}^3$ from the occupational exposure limits.

4.2 Evaluation of Existing Criteria

Ammonia is a substance with an unpleasant and pungent odour. Considering this aesthetic effect, both the point of impingement standard and the AAQC of Ontario were established based on the odour property of this substance.

Ammonia is corrosive and irritating. Exposure to high concentrations of ammonia can result in burns to the eyes, skin or lungs. However, the predominant acute and chronic effects of ammonia through the inhalation route of exposure are irritation and injury to the upper respiratory system in both humans and laboratory animals. From a health perspective, most of the agencies have established their air quality criteria based on the respiratory effects of ammonia.

Four of the six U.S. state agencies examined have based their guideline on the inhalation reference concentration (RfC) developed by the US EPA. An occupational study of workers in a soda ash plant (Holness *et al.*, 1989 as cited in US EPA, 1998) was employed in the RfC derivation. An animal study on rats (Brodersen *et al.*, 1976 as cited in US EPA, 1998) was used as supporting evidence for effects of ammonia on the respiratory system.

Table 1. Summary of Existing Air Quality Guidelines¹ for Ammonia

Agency	Guideline Value ²	Basis of Guideline	Date ³	Comments
US EPA (IRIS)	100 µg/m ³ (daily exposure over a lifetime)	Reference concentration (RfC); decreased pulmonary function	1991	NOAEL (HEC) adjusted with uncertainty factors
California (CAPCOA)	100 µg/m ³ (chronic annual)	US EPA RfC; respiratory, eye and skin irritation	1993	Noncancer chronic Reference Exposure Level
	2,100 µg/m ³ (acute 1-h reference exposure level); proposed acute REL: 3,200 µg/m ³	Human respiratory irritation concentration; eye and respiratory irritations in humans	1996	Noncancer Acute Reference Exposure Level
Massachusetts	100 µg/m ³ (annual average ambient level)	US EPA RfC;	1995	Allowable Ambient Limit
	100 µg/m ³ (24-hour ceiling limit)	US EPA RfC	1995	Threshold effects exposure limit
Michigan	100 µg/m ³ (24-hour average)	US EPA RfC	1991	Screening level
New Jersey	100 µg/m ³ (Maximum annual average)	US EPA RfC	1991	Ambient annual guideline concentration
New York	360 µg/m ³ (annual; AGC)	Occupational exposure limits; US EPA	1994	Chronic annual guideline
	4,000 µg/m ³ (1-hour average; SGC)	Occupational exposure limits	1994	Acute 1-hour average; ACGIH TLV-TWA
WHO	none		1987	No value found
Netherlands	120 µg/m ³ (annual MIC, maximum immission concentration)	Occupational exposure limits	1992	MAC of 18 mg/m ³ /150 (MAC from occupational limits)
Sweden	none		1993	No value found
Ontario	3,600 µg/m ³ (24-hour average)	Odour considerations	1985	Ambient Air Quality Criteria
	3,600 µg/m ³ (half-hour POI)	Odour considerations	1985	Point of Impingement

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Using conditions of 1 atmosphere and 20°C, 1 ppm = 0.708 mg/m³ (ATSDR, 1990).. Various agencies use conversion factors based on a range of temperatures, varying between 0°C to 25°C. Depending on the selected temperature, conversion of units may vary slightly.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

The US EPA considered the confidence in the principal study (Holness *et al.*, 1989) as medium. Although the sample size was relatively small and only male workers were studied, a free standing NOAEL (no-observed-adverse-effect level) of 6.4 mg/m^3 (9.2 ppm) was determined. The NOAEL was adjusted for the breathing rate of the workers (10 m^3 of air for an 8-hour shift) to that of the general population (20 m^3 of air per day) and for a discontinuous occupational exposure (a 5-day week) to a continuous environmental exposure (7-day week). Thus, a human equivalent concentration (HEC) of the NOAEL ($\text{NOAEL}_{\text{HEC}}$) of $2300 \text{ }\mu\text{g/m}^3$ was obtained. Uncertainty factors applied were 10 to account for the protection of sensitive individuals, and 3 for database deficiency (e.g. for the lack of chronic data, the proximity of the LOAEL to the NOAEL and the lack of reproductive and developmental toxicology studies). The uncertainty factor for database deficiency is not larger than 3 because it was shown that, in rats exposed to 32 ppm (23 mg/m^3) ammonia, no increases in blood ammonia levels were present, and only minimal increases occurred at $300 - 1000 \text{ ppm}$ ($212.4 - 708 \text{ mg/m}^3$) (Schaedel *et al.*, 1989 as cited in US EPA, 1998). This suggesting that no significant distribution of ammonia throughout the body is likely to occur at the human equivalent concentration calculated. Thus, a RfC of $100 \text{ }\mu\text{g/m}^3$ was derived.

In the supporting rat study (Broderson *et al.* 1976 as cited in US EPA, 1998), a LOAEL (lowest-observed-adverse-effect level) of $17,400 \text{ }\mu\text{g/m}^3$ (25 ppm) was identified for the increased severity of rhinitis, and pneumonia with respiratory lesions in the extra thoracic area. After adjusting for breathing rates (from animals to humans), and for the extra-thoracic gas:respiratory effect, a human equivalent concentration for the LOAEL ($\text{LOAEL}_{\text{HEC}}$) of $1900 \text{ }\mu\text{g/m}^3$ (2.7 ppm) was calculated. The US EPA (1998) explained that there was a concentration-response relationship in the extra-thoracic region in experimental animals, beginning at a LOAEL which was essentially the same human equivalent concentration (HEC) as the NOAEL in the study of Holness *et al.* (1989).

The agency of California recently proposed an acute reference exposure level of $3200 \text{ }\mu\text{g/m}^3$ based on the irritation effects of ammonia to the eyes and the respiratory system. Four human studies were evaluated (Silverman *et al.*, 1949; MacEwen *et al.*, 1970; Industrial Biotest Laboratories, 1973 and Verberk, 1977 all cited in OEHHA, 1998). The acute REL was estimated with a benchmark concentration (BMC) approach, using a log-normal probit analysis method (Crump and Howe, 1983 and Crump, 1984 as cited in OEHHA, 1998). The maximum likelihood estimate (MLE) for a 5% response was calculated to be 20.1 ppm (14.2 mg/m^3). The 95% lower confidence limit (LCL) of the BMC_{05} was determined to be 13.6 ppm (9.6 mg/m^3). This was defined as the Benchmark concentration which corresponded to a response rate of 5%. A safety factor of 3 was applied to this BMC_{05} value to protect sensitive individuals and, a final acute REL of 4.5 ppm ($3200 \text{ }\mu\text{g/m}^3$) was obtained.

The short-term guideline concentration of $4000 \text{ }\mu\text{g/m}^3$ of New York was derived from the threshold limit value-time weighted value (TLV-TWA) of 25 ppm (17 mg/m^3) of the American Conference of

Governmental Industrial Hygienists (ACGIH) whereas the annual guideline concentration of 360 µg/m³ was adopted from the US EPA. No documentation is available to validate this derivation.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including ammonia, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationales of the agencies that the Ministry has considered appropriate for the development of air quality standards; specifically the use of the RfC of the US EPA and the acute REL of the California EPA and technical and economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received five submissions from various stakeholders regarding the draft document for ammonia. A rubber industry stakeholder commented that it would be possible to meet a revised standard at a value six-fold lower than the current POI guideline and a greater than 10-fold reduction may be achieved by increasing the emission stack height. Comments from a chemical industry stakeholder anticipated little or no change in the air quality standards for ammonia and indicated that costly improvement in pollution control had recently been installed and further equipment upgrades had been planned to reduce the release of ammonia from its facility. An automobile parts and accessory manufacturer stakeholder suggested that the US EPA's RfC and the REL from the California EPA would appear to be the most appropriate for air quality standards derivation. One paint chemical manufacturing facility requested clarification on the rationale for revision of air quality standards. One chemical producing stakeholder provided additional research information for risk assessment.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The comments from stakeholders received during the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide additional information such as any technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard, which are presented in Section 8.0 below. This is the next phase in the

overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for ammonia. If attainment of the proposed standard cannot be achieved immediately, this phase will be followed by a third phase in which risk management options are discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted, depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for Ammonia

The existing ambient air quality criterion for ammonia in Ontario is $3600 \mu\text{g}/\text{m}^3$ (24-hour average). The point of impingement standard is also $3600 \mu\text{g}/\text{m}^3$. Both values are based on odour/irritation as a limiting effect.

Ammonia is a corrosive substance which can act as a respiratory irritant. Human and animal studies indicate that the predominant adverse health outcomes from exposure to ammonia is irritation and injury to the upper respiratory system and eye irritation. The majority of agencies have adopted the RfC of $100 \mu\text{g}/\text{m}^3$, developed by the US EPA, as an appropriate exposure limit for ammonia. The RfC is derived principally from an occupational study which defined a no-adverse-effects-level of $6400 \mu\text{g}/\text{m}^3$. The RfC incorporates adjustments for the difference in breathing rate and duration of exposure between occupationally exposed individuals and the general public, resulting in a combined uncertainty factor of 30.

Consistent with the long-term corrosive and irritant effects of ammonia in humans and in animals through inhalation exposure, the RfC of $100 \mu\text{g}/\text{m}^3$, developed by the US EPA, is considered sufficient for the protection of human health. The merit of using this air quality criterion as the basis for the derivation of air quality standards for Ontario, is that the studies used by the U.S. EPA were highly relevant human studies. The uncertainty factors employed in its criterion derivation were reasonable.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the Reference

Concentration established by the US EPA. After reviewing additional toxicological information, the Ministry considers the uncertainty factors used by the US EPA to derive its RfC, reasonable. Therefore, a 24-hour AAQC of $100 \mu\text{g}/\text{m}^3$ based on the RfC is proposed. The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b)

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for ammonia:

- **a 24-hour average AAQC of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ammonia based on the adverse health effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $300 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $3600 \mu\text{g}/\text{m}^3$ to this revised level of $300 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$300 \mu\text{g}/\text{m}^3$ to $3,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ammonia.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and

reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in

accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;

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- MOE Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects" Economic Services Branch- April 1994, and;
 - "Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for ammonia can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Ammonia

2. *Agency:* U.S. Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. There is a reference concentration (RfC) of 100 $\mu\text{g}/\text{m}^3$ for chronic inhalation exposure in the IRIS database (US EPA, 1997; last review 01/05/91). No carcinogenicity assessment was done.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

Key Reference(s):

Broderson, J.R., J.R. Lindsey and J.E. Crawford. 1976. The Role of Environmental Ammonia in Respiratory Mycoplasmosis of Rats. *Am. J. Pathol.*, 85: 115-130.

Dahlman, T. 1967. Mucus Flow and Ciliary Activity in the Trachea of Healthy Rats Exposed to Respiratory Irritant Gases (SO_2 , NH_3 and HCHO) - A Functional and Morphologic (Light Microscopic and Electron Microscopic) Study, with Special Reference to Technique: VIII. The Reaction of the Tracheal Ciliary Activity to Single Exposure to Respiratory Irritant Gases and Studies of the pH. *Acta Physiol. Scand.*, 36 (Suppl. 123): 93-97.

Flury, K.E., D.E. Dines, J.R. Rodarte and R. Rodgers. 1983. Airway Obstruction Due to Inhalation of Ammonia. *Mayo Clin. Proc.*, 58: 389-393.

Gamble, M.R. and G. Clough. 1976. Ammonia Build-up in Animal Boxes and its Effect on Rat Tracheal Epithelium. *Lab. Anim.*, 10: 93-104.

Holness, D.L., J.T. Purdham and J.R. Nethercott. 1989. Acute and Chronic Respiratory Effects of Occupational Exposure to Ammonia. *Am. Ind. Hyg. Assoc. J.*, 50: 646-650.

Schaerdel, A.D., W.J. white, C.M. Lane, B.H. Dvorchik and K. Bohner. 1983. Localized and systemic effects of environmental ammonia in rats. *Lab. Anim. Sci.* 33: 40-45.

Schoeb, T.R., M.K. Davidson and J.R. Lindsey. 1982. Intracage Ammonia Promotes Growth of *Mycoplasma Pulmonis* in the Respiratory Tract of Rats. *Infect. Immun.*, 38: 212-217.

6. Peer Review Process and Public Consultation:

US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based U.S. regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

No guidelines exist. The risk estimate discussed is for respiratory exposure from air only.

8. Key Risk Assessment Considerations:

The US EPA (1997) has calculated a RfC which considers toxic effects for which a threshold exists. The RfC for ammonia was calculated using results from the principal study: an investigation of occupational exposure at a soda ash facility (Holness *et al.*, 1989). Based on this study, EPA estimated a time-weighted average (TWA) no observed adverse effect level (NOAEL) of 6,400 $\mu\text{g}/\text{m}^3$ (9.2 ppm). Adjustment for the TWA from an occupational setting to a continuous environmental exposure resulted in a NOAEL for a human equivalent concentration (HEC) of 2,300 $\mu\text{g}/\text{m}^3$. (Note: factors considered in the adjustment included a breathing volume of 10 m^3 of air per 8-hour shift for the workers as compared to a daily breathing volume of 20 m^3 for the general population; a 5-day work-week for the workers as compared to a 7-day week for the general population. Therefore, the $\text{NOAEL}_{\text{HEC}}$ was derived according to the following: $6,400 \mu\text{g}/\text{m}^3 \times 10/20 \times 5/7 = 2,300 \mu\text{g}/\text{m}^3$). An uncertainty factor of 10 was applied to allow for sensitive populations and a factor of 3 was used to account for the incompleteness of the database. The inhalation RfC was therefore estimated to be 100 $\mu\text{g}/\text{m}^3$ (2.3 mg per $\text{m}^3/30$). The critical effect of this research was a lack of evidence of decreased pulmonary function or subjective symptomology. However, there are some uncertainties about this study: exposed workers reported aggravated specific symptoms including coughing, wheezing, nasal complaints, eye irritation, throat discomfort and skin problems. No objective investigation of the worker's nasal epithelium was performed. There are also some questions about selection bias against atopic dispositions as suggested by the lower prevalence of allergy symptoms in both the exposed and

control groups which refers to the probably hereditary allergy characterized by symptoms. In addition, the sample size was small ($n=53$) and composed only of men (all references in above paragraph as cited in US EPA, 1998).

The RfC is supported by the Broderson *et al* (1976) animal study. F344 rats were exposed to 0, 25, 50, 150 or 250 ppm ammonia (continuously) for 7 days prior to inoculation with *Mycoplasma pulmonis*. A-Lowest-Observed-Adverse-Effect Level (LOAEL)-human equivalent concentration (HEC) was identified as $1,900 \mu\text{g}/\text{m}^3$ for an increased severity of rhinitis and pneumonia respiratory lesions. These results are consistent with those of another study involving F344 rats (Schoeb *et al.*, 1982).

On comparing the Holness study with all other data on the respiratory effects of ammonia in humans and animals, the US EPA observes a trend that at low concentrations, the extra thoracic region of the respiratory system is affected due to the chemical solubility and reactivity, while at higher concentrations, the lower part of the respiratory system is involved in both experimental animals (Dahlman, 1956; Gamble and Clough, 1976) and humans (Flury *et al.*, 1983). Thus, at low exposure levels, no effects were observed in the lower respiratory system as reflected by pulmonary function, while the complaint of the exacerbated upper respiratory symptoms suggest sensory irritation and support the extra thoracic region as the critical region for an effect.

From these results, the EPA concludes that there is a concentration-response relationship in the extra thoracic region in experimental animals beginning at a LOAEL at essentially the same HEC as the NOAEL in Holness *et al.* (1989) and the NOAEL may be based on a less sensitive endpoint.

Although ammonia has not been tested adequately for its reproductive and developmental toxicity, the NOAEL is very close to the LOAEL. Despite the weakness of the primary study, the uncertainty factor was not set at a higher level because studies in rats (Schaerdel *et al.* 1983) suggest that no significant distribution of ammonia is likely to occur at the HEC level calculated.

9. Key Risk Management Considerations:

None, since no guidelines exist for ambient air.

10. Multimedia Considerations of Guidelines:

None are reported.

11. Other Relevant Factors:

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Ammonia

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The reference exposure level of $100 \mu\text{g}/\text{m}^3$ is to be used for assessing chronic non-cancer risks while the reference level for acute exposure is $2,100 \mu\text{g}/\text{m}^3$. Recently, the OEHHA has proposed an acute REL of $3,200 \mu\text{g}/\text{m}^3$. Chronic exposure reference level should be compared with modelled annual average air concentrations while acute non-cancer reference levels should be compared with modelled 1-h average concentrations.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' Program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritized. These guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and re-submission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

Key Reference(s):

Lewis, D.C. and G. V. Alexeeff. 1989. Quantitative Risk Assessment of Non-cancer Health Effects for Acute Exposure to Air Pollutants. *In:* Proceedings of the Air and Waste Management Association 82nd Annual Meeting, June 1989, Vol. 89-91.

OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Ammonia. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

US EPA, 1998. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

The guideline is current, but updates using new California risk assessment guidelines are being considered in the California Senate.

8. Key Risk Assessment Considerations:

California agrees with the EPA's RfC of $100 \mu\text{g}/\text{m}^3$ as its Reference Exposure Level (chronic).

The non-cancer acute reference exposure level (REL) for inhalation of $2,100 \mu\text{g}/\text{m}^3$ is based on human respiratory irritation using the Defined Practical Threshold (DPT) methodology proposed by Lewis and Alexeeff (1989). Four human data sets were integrated, log-probit analysis was used to model the combined dose response slope, and the benchmark dose (BMD) was estimated for a 1% increase in irritation response with a 95% lower confidence limit on dose. No modifying factors were applied. The obtained value should protect against perceptible occurrence of observable effects, including irritation, among an exposed human population for a one-hour exposure. Recently, the OEHHA has proposed a revised acute REL of $3,200 \mu\text{g}/\text{m}^3$, based on four short-term studies on human volunteers. A benchmark concentration at a 95% lower confidence limit (BMC_{05}) was derived. These studies include:

Seven volunteers were exposed to ammonia at 500 ppm ($355 \text{ mg}/\text{m}^3$) for 30 min. using an oral-nasal mask (Silverman *et al.*, 1949 as cited in OEHHA, 1998). Although the reported symptoms varied widely, upper respiratory irritation was noticed for all test subjects. Irritation was graded as severe in

two volunteers. Only two subjects were able to continue nasal breathing throughout the 30 minute exposure. Responses included irritations of the nose and throat, hypoesthesia of the exposed skin, and lacrimation. In two subjects, the nasal-pharyngeal irritation persisted for 24 hours following the exposure. One of the volunteers was exposed for only 15 minutes rather than the 30 min. full exposure and the reason for this exposure period deviation was not known.

In another human study eight subjects with previous exposures and eight subjects with no previous exposures (naive group) were exposed to ammonia for two hours at concentrations of 50, 80, 110 and 140 ppm (36, 57, 78 and 99 mg/m³, respectively) (Verberk, 1977 as cited in OEHHA, 1998). The group with no previous exposures could not tolerate the 99 mg/m³ concentration for two hours and had several complaints during exposure to 78 mg/m³ for one hour. None of the volunteers demonstrated a decrease in measured pulmonary function tests, including the vital capacity, forced expiratory volume (1 second) and the forced inspiratory volume (1 second) following ammonia exposure. The results showed a greater sensitivity to ammonia for the naive group in smell, eye irritation, cough, general discomfort, headache and irritation of the chest. At the end of the initial 30 min. of the 2-hour period of exposure, nuisance level of smell, eye, nose or throat irritation or cough urge were reported by 7 of 16 (44%), 9 of 16 (56%), 12 of 16 (75%) or 15 of 16 (94%) subjects at 36, 57, 78 or 99 mg/m³, respectively.

Groups of five and six volunteers were exposed to respective ammonia concentrations of 30 and 50 ppm (21 and 36 mg/m³) for 10 min. (MacEwen *et al.*, 1970 as cite in OEHHA, 1998). No moderate or higher irritation was discerned by the group at the lower exposure group. However, four of the six subjects rated the 10-min. exposure at 36 mg/m³ as causing moderate irritation.

Ten test human subjects were exposed to ammonia at 32, 50, 72 and 134 ppm (23, 36, 51 and 95 mg/m³, respectively) (Industrial Bio-Test Laboratories, 1973 as cited in OEHHA, 1998). Irritation was reported as any annoyance of the eyes, nose, mouth, throat or chest which persisted throughout the 5-minute exposure period. Three subjects reported eye irritation at 51 mg/m³, two had nasal irritation and three had throat irritation. At 95 mg/m³, five of the ten subjects experienced lacrimation and eye irritation, seven complained of nasal irritation and eight had throat irritation and one complained of chest irritation.

It was calculated that the maximum likelihood estimate (MLE) for a 5% response was 20.1 ppm (14.2 mg/m³) and the 95% LCL on this value (BMC₀₅) for ammonia from the analysis was 13.6 ppm (9.6 mg/m³). The Office of Environmental Health Hazard of California considered only an uncertainty factor of 3 to protect sensitive individuals. Thus, an acute REL was calculated as 4.5 ppm (3.2 mg/m³; 3200 µg/m³). This acute REL was supported by a parallel BMC analysis using several animal studies.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population. For ammonia, the effect is irritation and injury to the respiratory system.

The State of California allows local options to address the possible economic impacts of ammonia emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993). Ammonia is not one of the substances requiring non-inhalation modelling.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Ammonia

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

Both the Threshold Effects Exposure Limit (TEL; 24-hour average) and the Allowable Ambient Limit (AAL; annual average) are $100 \mu\text{g}/\text{m}^3$. It is stated in the latest revised edition (1995) that "in cases where the TEL equals the AAL, the TEL concentration and averaging time should be used."

4. *Application:*

"... The Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Key Reference(s):

US EPA, 1994. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was employed. As guidelines, the process used and values generated are not subjected to, but external peer reviews were carried out, and public input was solicited through at least two public meetings on the Massachusetts methodology and guideline document (Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE Staff). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each individual AAL will undergo review a minimum of every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

For ammonia, the Massachusetts Department of Environmental Protection agrees with the US EPA's RfC of $100 \mu\text{g}/\text{m}^3$ as its Allowable Ambient Limit (AAL) and its Threshold Effects Exposure Limits (TEL). TELs are exposure limits based on threshold health effects while AALs are based on both threshold and non threshold health effects. The DEP decision to incorporate the RfCs permits a way to consider "recent peer-reviewed toxicity information on the threshold effects of a compound while maintaining the same degree of health protection afforded by the CHEM/AAL methodology" (ORS, 1994). Because ammonia is not considered as a carcinogen, (non-threshold exposure limit equals 1) both AAL and TEL are set to $100 \mu\text{g}/\text{m}^3$. However, the note attached to the revised list mentions specifically that "in cases where the TEL equals the AAL, the TEL concentration and averaging time should be used".

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

10. Multimedia Considerations of Guidelines:

Prior to revised methodology, a factor of 20% was systematically applied as a relative source contribution factor. However, the 1994 revision states that "the multi-media exposure factor is not used with water soluble gases (i.e., NH_3 , H_2S and HCL) since it is assumed that exposure to these compounds is largely via inhalation and they are mainly respiratory toxicants." (ORS, 1994).

11. *Other Relevant Factors:*

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Ammonia

2. *Agency:* Michigan (Department of Natural Resources)

3. *Guideline Value(s):*

The Screening levels (Initial Threshold Screening Level; ITSL) in Michigan is $100 \mu\text{g}/\text{m}^3$.

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxics rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. Then, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

Michigan Department of Natural Resources, 1995/1997. Air Toxics Screening Levels. Air Quality Division. 6p. + Appendices

Key Reference(s):

US EPA, 1996. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months while a complete list of all screening levels is published once a year.

8. *Key Risk Assessment Considerations:*

When the US EPA establishes an RfC, it is then used to define the ITSL. For ammonia, Michigan agrees with US EPA's RfC of $100 \mu\text{g}/\text{m}^3$ because it is not considered as a carcinogen. For other chemicals, reference screening levels can be obtained from various other agencies

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Ammonia

2. *Agency:* New Jersey

3. *Guideline Value(s):*

The reference concentration for inhalation in New Jersey is $100 \mu\text{g}/\text{m}^3$.

4. *Application:*

The list of reference concentrations for inhalation is maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. The reference concentrations do not appear to be legally enforceable because the Air Quality Permitting Program Risk Management Committee can issue a final case-by-case review and recommendation regarding permitting of the source after it has failed a first and a second level risk screening. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.). However, if the hazard index calculated is higher than one, the risk is evaluated on a case-by-case basis.

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

In the case of non-carcinogens, the RfC is directly used in the risk assessment or screening procedures. For Ammonia, New Jersey agrees with US EPA's RfC of $100 \mu\text{g}/\text{m}^3$. For other chemicals, different agencies can be used to obtain reference concentrations. New Jersey believes that it is not because a

chemical has not shown carcinogenicity that it is a proven non-carcinogen. As such, ammonia is listed as no data available, as no conclusion can yet be reached on its carcinogenicity.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Ammonia

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC; 1-h average air concentration) is 4,000 $\mu\text{g}/\text{m}^3$ and the annual Guideline Concentration (AGC) is 360 $\mu\text{g}/\text{m}^3$.

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

Key Reference(s):

American Conference of Governmental Industrial Hygienists, 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

6. *Peer Review Process and Public Consultation:*

The scientific documents prepared by the New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guidelines development process, but specific information on the process for ammonia was not presented in the available documentation.

7. *Status of Guideline:*

Current.

8. Key Risk Assessment Considerations:

New York State (1991) has classified the toxicity of ammonia as low. Compounds given the designation of low are "those chemicals that might cause irritation or reversible effects to sensitive members of the population, and which do not meet the criteria for classification as HIGH or MODERATE toxicity contaminants". The short-term guideline concentration for this class of chemicals is currently under review and no additional information is available on the procedure used to derive the actual concentration. It is, however, stated that the short-term guideline for ammonia is derived from the TLV-TWA (ACGIH, 1990-1991). The long term guideline was derived from EPA sources (information not available). No additional information is given as to the actual process followed to arrive at the current guideline value.

9. Key Risk Management Considerations:

A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses as employed in the permitting process. Presently, the latest version of Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

No information.

11.7 Agency-Specific Summary: World Health Organisation (WHO)

1. *Name of Chemical:* Ammonia

2. *Agency:* World Health Organisation

3. *Guideline Value(s):*

None.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426p.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

No information.

11.8 Agency-Specific Summary: The Netherlands.

1. *Name of Chemical:* Ammonia

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

A value of 120 $\mu\text{g}/\text{m}^3$ has been estimated for the MIC (Maximum Immission Concentration) for ammonia by dividing the MAC (Maximum Acceptable Concentration) of 18,000 $\mu\text{g}/\text{m}^3$ by 150. The MAC is based on occupational limits which are used when no environmental data are available.

4. *Application:*

Limit values are non-statutory environmental quality objectives that are considered policy guidelines. They should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effect-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effect-oriented guidelines.

The target value is the level at which the risk of adverse effects to the ecosystem, functional properties of the environment or other compartments are considered negligible. It is the final objective for the environmental quality to be met in the Netherlands and, as such, might eventually become similar to the limit value.

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A Review of Environmental Quality Objectives and Their Policy Framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 pp. + Appendices.

Key Reference(s):

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances such as ammonia, but only in Dutch.

6. *Peer Review Process and Public Consultation:*

No specific information on this issue was presented in the available English documentation.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

Ammonia has been placed on a priority list of chemicals requiring special attention. The list of priority substances and an integrated document containing all relevant data needed to determine any risk were scheduled for revision and preparation early in 1994.

The national guidelines issued are derived from occupational hygiene limit values (MAC values) dating from 1992. The reported MAC values are TWA values (eight hours a day, 40 hours a week). It is stated that "when these values are set, the principle is used that repeated exposure to that concentration during longer periods, even as much as a full working life, should generally not affect the health of workers or their children." For ammonia, the target MIC value (Maximum Immission Concentration for air polluting components in the outdoor air and inhabited level) of $120 \mu\text{g}/\text{m}^3$ is derived directly from the MAC value ($18,000 \mu\text{g}/\text{m}^3$). Because ammonia is not considered carcinogenic, the MAC value is simply divided by a factor of 150. The value of 150 appears, according to the compilers of the MIC values, to be closest to air pollution criteria based on scientific research. The source of this information is available only in Dutch.

9. *Key Risk Management Considerations:*

MAC values are not solely based on health consideration. In fact, national limit values include consideration of environmental, economic and social interests as well as technical options. Specific information on such details was not presented in the available documentation.

10. *Multimedia Considerations of Guidelines:*

Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. A specific schedule for revisions based on this process has not been announced and ammonia is not on the initial list of chemicals to be considered.

11. *Other Relevant Factors:*

No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. Name of Chemical: Ammonia

2. Agency: Swedish Environmental Protection Agency

3. Guideline Value(s):

No guidelines.

4. Application:

No information.

5. Documentation Available:

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. Chemosphere 27: 1691-1706.

Victorin, K., 1997. Personal communication.

Key Reference(s):

None.

6. Peer Review Process and Public Consultation:

No information.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

No information.

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.10 Agency-Specific Summary: Canada (CEPA)

1. *Name of Chemical:* Ammonia

2. *Agency:* Environment Canada

3. *Guideline Value(s):*

No information.

4. *Application:*

No information.

5. *Documentation Available:*

Canadian Environmental Protection Act (CEPA), 1993-94. CEPA Priority Substance List (PSL) 1.
Environment Canada and Health and Welfare.

Key Reference(s):

A revision has been initiated (PSL 2), but no preliminary document is yet available.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RFC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
CHLORINE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Chlorine was identified as a priority compound for review based on its pattern of use in Ontario as well as the toxicological information that has been published subsequent to the development of the existing standard in 1984. A review of the scientific and technical information relevant to setting an ambient air quality standard for chlorine has previously been provided to stakeholders for their comment. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for chlorine.

Chlorine (CAS # 7782-50-5) is a greenish-yellow gas, liquid, or rhombic crystals. It has a suffocating odour with odour thresholds ranging from 0.021 - 3.4 ppm (61 - 9860 $\mu\text{g}/\text{m}^3$). It is used in the production of chlorinated solvents, chlorofluorocarbons, propylene oxide, pesticides, ethylene dichloride, and in special batteries that contain lithium or zinc. It is used as an intermediate for vinyl chloride monomer and polyvinyl chloride resin production. In the paper industry chlorine is used to bleach pulp. It is used in shrink-proofing wool. It is used in special batteries that contain lithium or zinc. Chlorine serves as a disinfectant or fungicide for applications such as water purification, cooling systems, and food processing, including meat, fish, vegetables, and fruit.

Chlorine is rapidly absorbed into the blood following exposure and is excreted from the body mainly through urination and defecation. It is considered moderately toxic and very irritating to humans when inhaled. Inhalation affects the respiratory system causing tracheal and bronchial changes, emphysema, chronic pulmonary edema, and congestion. Chlorine is also a strong irritant to the eyes and mucous membranes. The respiratory tract and the blood are the organ and tissue most affected by subchronic or chronic exposure to chlorine. Due to limited information concerning human and animal studies, the US Environmental Protection Agency (US EPA) has not drawn any conclusion on the carcinogenicity, developmental, or reproductive toxicity of chlorine.

Data obtained from the National Pollutant Release Inventory (NPRI) provided by Environment Canada indicates that emissions of chlorine to air across Canada declined significantly from 4153 tonnes in 1993 to 909.5 tonnes in 1997. Atmospheric emissions of chlorine in Ontario showed a similar decline. The most significant decreases in Ontario occurred between 1993 and 1994, when releases of chlorine declined from 1554 tonnes in 1993 to 181 tonnes in 1994. The release of chlorine in Ontario was reported to be 142 tonnes in 1997.

Neither Environment Canada nor the MOE routinely monitor ambient air for chlorine. The highest level recorded, during monitoring performed by the MOE in 1995, was under 200 $\mu\text{g}/\text{m}^3$ of chlorine (half-

hour average) and was in the vicinity of a foundry in the Greater Toronto Area. In September 1991, near an aluminum plant in Windsor, the half-hour average concentrations were found to be around the detection limits of 0.28 - 0.44 $\mu\text{g}/\text{m}^3$.

The current half-hour POI standard for chlorine is 300 $\mu\text{g}/\text{m}^3$ and is based on health effects. The current 24-hour AAQC is 150 $\mu\text{g}/\text{m}^3$ and is based on the health and vegetation effects of chlorine.

In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan and the Commonwealth of Massachusetts; the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. The States of California, Michigan, New Jersey, New York and the Commonwealth of Massachusetts have promulgated air quality guidelines or reference exposure levels for chlorine based on occupational exposure limits.

Current ambient air quality criteria from the U.S. state agencies are derived from occupational exposure limits. The different values are due to the varying uncertainty factors used in their derivation. The acute exposure limits of these agencies vary between 15 and 350 $\mu\text{g}/\text{m}^3$ and chronic exposure guidelines vary between 3.5 and 7.1 $\mu\text{g}/\text{m}^3$. The half-hour average emission guideline for The Netherlands is 5000 $\mu\text{g}/\text{m}^3$, which was established for permitting uses.

The State of California is proposing a revised acute Reference Exposure Level (REL) of 210 $\mu\text{g}/\text{m}^3$ based on irritation to humans as well as a chronic REL of 0.06 $\mu\text{g}/\text{m}^3$ based on respiratory effects of chlorine in animals. The Ministry considers that California's proposed RELs are derived from the most current information available and have addressed the health concerns of this compound. However, the Ministry considers that an in-depth evaluation of this information is appropriate only after the peer review process for these RELs are complete.

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and accepts the rationale which supports the current occupational exposure limit of 1,500 $\mu\text{g}/\text{m}^3$ (0.5 ppm) from the American Conference of Governmental Industrial Hygienists. After exposure averaging time conversion and the application of uncertainty factors, a 24-hour AAQC of 10 $\mu\text{g}/\text{m}^3$ has been derived.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for chlorine:

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- a 24-hour average AAQC of $10 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine based on the health effects of this compound; and,
 - a 10 -minute AAQC of $230 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine based on the odour nuisance of this compound.

Based on supporting science and dispersion modelling, a half-hour POI standard of $30 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $300 \mu\text{g}/\text{m}^3$ to this revised level of $30 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- $30 \mu\text{g}/\text{m}^3$ to $300 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine.

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Chlorine was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing standard in 1984. A review of scientific and technical information relevant to setting an ambient air quality standard for chlorine had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for chlorine.

2.0 General Information

2.1 Physical and Chemical Properties

The following list provides some general information on chlorine and its properties:

CAS #	7782-50-5
RTECS #	FO2100000
UN #	1017
Conversion Factors	1 ppm = 2.9 mg/m ³ @ 25 °C and 1 atm 1 mg/m ³ = 0.34 ppm @ 25 °C and 1 atm
Boiling Point	-34.05 °C at 760 mm Hg
Flash Point	Nonflammable
Henry's Law Constant	No data
Log K _{OW}	No data
Formula	Cl ₂
Molecular Weight	70.90 g/mol
Vapour Density (air = 1)	3.21 mg/L at 0 °C and 1 atm
Vapour Pressure	5850 mm Hg @ 25 °C
Common Synonyms	None

Chlorine is a greenish-yellow gas, liquid, or rhombic crystals (Lewis, 1992). It has a suffocating odour with odour detection thresholds range from 0.021 - 3.4 ppm (61 - 9860 µg/m³) while the geometric mean for the odour detection thresholds is 0.08 ppm (232 µg/m³) (AIHA, 1989)

2.2 Uses of Chlorine

Chlorine is used in the production of chlorinated solvents, chlorofluorocarbons, propylene oxide, pesticides and ethylene dichloride and as an intermediate for vinyl chloride monomer and polyvinyl chloride resin production. In the paper industry, chlorine is used to bleach pulp. It is used in shrink-proofing wool and in special batteries that contain lithium or zinc. Chlorine serves as a disinfectant or fungicide for applications such as water purification, cooling systems, and food processing, including meat, fish, vegetables, and fruit. Chlorine's disinfectant and fungicidal properties are also used in foot baths, dairy equipment, laundries, and dishwater (US EPA, 1994).

2.3 Sources and Levels

Sources

Chlorine is a naturally occurring element which, is also produced industrially (US EPA, 1994). Environment Canada's National Pollutant Release Inventory (NPRI) summarizes the emissions of chemicals in Canada based on information provided by reporting facilities. Chlorine is among the top 25 pollutants released to air (NPRI, 1995). Based on the summary reports of 1993 to 1997, total releases of chlorine in Canada have declined significantly, from 4153 tonnes in 1993 to 2034, 1244, 916 and 909.5 tonnes in 1994, 1995, 1996 and 1997, respectively (NPRI 1993; NPRI, 1994; NPRI, 1995, NPRI, 1996 & NPRI, 1997). The total releases in Ontario showed a similar pattern. In 1993, 1554 tonnes of chlorine were released, this amount decreased significantly to 181, 170, 144 and 142 tonnes in 1994, 1995, 1996 and 1997, respectively. The 1997 NPRI report listed 16 sources of atmospheric release of chlorine in Ontario, the vast majority of these releases were from forestry product industries.

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 26 facilities that emit chlorine were identified. These approvals were from emission sources from the forest product and mining industries, disinfectant uses and chemical plants. The median Ground Level Concentration (GLC) estimated by Regulation 346 dispersion modelling for all 26 sources was approximately $3 \mu\text{g}/\text{m}^3$. The maximum and minimum were 301 and $0.00035 \mu\text{g}/\text{m}^3$, respectively.

Ambient Air Concentrations

Environment Canada does not routinely monitor ambient air for chlorine. Monitoring undertaken in September 1991 found half-hour average concentrations to be around the detection limits of $0.28 - 0.44 \mu\text{g}/\text{m}^3$, near an aluminum plant in Windsor (MOEE, 1994b). In 1995, the highest levels detected, of chlorine, were in the vicinity of a foundry in the Greater Toronto Area and were under $200 \mu\text{g}/\text{m}^3$ (MOEE, 1997).

2.4 Environmental Fate

Vaporization of chlorine from water into the atmosphere is insignificant at neutral pH and low concentrations, but becomes significant at low pH values (i.e., pH 2) and high chlorine concentrations ($\sim 3,500 \text{ mg}/\text{L}$) (US EPA, 1994). Chlorine can play a role in the formation of photochemical oxidants (particularly nitric acid and sulphate), via the production of hydroxyl radicals, as shown in an industrialized area of Norway (Hov, 1984).

Chlorine may react with soil components to form chlorides which may be washed from the soil, depending on their water solubility (US EPA, 1994). Rapid hydrolysis of chlorine occurs in water, as the half-life of chlorine in natural waters is 0.005 seconds (US EPA, 1994). Chlorine does not bioaccumulate or bioconcentrate in biota (HSDB, 1994).

3.0 Toxicology of Chlorine

The following toxicological review of chlorine is primarily focussed on the inhalation route of exposure, as this is a primary pathway of human exposure to chlorine in air. Data on other exposure media are included where relevant, or where inhalation data are lacking.

Chlorine is rapidly absorbed into the blood following oral administration. It has been found that chlorine concentrations in rats peaked in two hours for fasted animals and in four hours for nonfasted animals (US EPA, 1994). Seventy-two hours after oral administration the concentration of chlorine was highest in the plasma, followed by bone marrow, kidney, testes, lung, skin, duodenum, spleen, liver, and carcass. The lowest concentration was found in the ileum. Similar results were observed 96 hours after a dose of 2.61 mg/kg was administered (US EPA, 1994). Once absorbed, free chlorine (Cl_2 , OCl^- , or HOCl) is a powerful oxidizing agent that reacts readily with biological materials to produce a number of chlorinated organic compounds. Chlorine is excreted from the body mainly through urination and defecation. Rats given oral doses of chlorine excreted 36.4% in their urine and 14.8% in their faeces within 96 hours of dose administration. Chlorine compounds were not detected in expired air (US EPA, 1994).

3.1 Acute Toxicity

In general, chlorine is moderately toxic but very irritating to humans if inhaled. Inhalation of chlorine effects the respiratory system causing tracheal and bronchial changes, emphysema, chronic pulmonary edema, and congestion. It is also a strong irritant to the eyes and mucous membranes (Lewis, 1992). The extent of acute chlorine injury to humans is dependent, not only on the concentration and length of exposure, but also on the water content of the exposed tissue and the presence of a pre-existing cardiopulmonary disease. Clinical effects of different chlorine concentrations include mild mucous membrane irritation at 2.9-8.7 mg/m^3 , which worsens to moderate irritation of the upper respiratory tract at concentrations of 14.5-43.5 mg/m^3 . Immediate chest pain, vomiting, dyspnea, and cough occur at 87 mg/m^3 , toxic pneumonitis and pulmonary edema at 116-174 mg/m^3 , and death occurs after 30 minutes exposure to 1,247 mg/m^3 or after a few minutes at 2,900 mg/m^3 (US EPA, 1994).

A study on 29 volunteers of men and women, composed of smokers and non-smokers, were exposed to chlorine at 0, 0.5 or 2 ppm (0, 1.45 or 5.8 mg/m^3) for 4- or 8-hour periods (Anglen, 1981 as cited

in OEHHA, 1998). Test subjects recorded their reactions upon entering the chamber at 15-, 30-, 60-, 90-, 120-, 180- and 240-minute intervals. Significant sensations of the urge to cough, itching and burning of the nose and eyes, and general discomfort were reported at or above 1 ppm (2.9 mg/m³). A few subjects reported mild sensations of nausea, headache, dizziness, drowsiness or shortness of breath at the end of the 8-hour exposure period at 1 ppm (2.9 mg/m³). There were significant changes in pulmonary function and increased subjective irritation at 1 ppm (2.9 mg/m³), pulmonary functional changes were not observed at 0.5 ppm (1.45 mg/m³) for the 8-hour exposure period and the subjective irritation was less severe. Medical examinations of the subjects indicated that there were some significant changes during the 8-hour exposure period at concentrations above 1 ppm (2.9 mg/m³), such as increased mucous secretion from the nose and in the hypopharynx.

The ACGIH reviewed another study which reported that 8-hour exposures at 0.5 ppm (1.45 mg/m³) produced irritation in workers. A study of 332 male workers in 25 chloralkali plants matched with 382 workers not exposed to chlorine was referenced in the ACGIH background documentation for chlorine. TWA exposure data were calculated for each worker on an 8-hour basis. Chlorine concentrations in the air were sampled every 2 months at different locations, within each of the plants participating in the study. All but 6 of the workers were reported to have exposures below 1 ppm, and 21 had TWAs above 0.52 ppm, the concentration of chlorine ranged from 0.006 to 1.42 ppm, with an average of 0.15 ppm. The average chlorine exposure was 10.9 years. Of 329 electrocardiograms from 332 workers, 9.4 % were abnormal compared with 8.5 % in the 382 controls, this was not considered a significant difference (ACGIH, 1991). The incidence of fatigue was greater in workers exposed to levels above 0.5 ppm, anxiety and dizziness showed a modest correlation with exposure level, however no neoplasia or serious permanent pulmonary damages were noted (ACGIH, 1991).

3.2 Subchronic/Chronic Toxicity

The respiratory tract and blood are the most affected by subchronic/chronic exposures to chlorine. In 55 workers, asthma, chronic bronchitis, tuberculosis, and emphysema were the result of chlorine exposure at 2.9 mg/m³ for a minimum of ninety 8-hour work days. In another study of 15 male workers, exposed to 0.5 mg/m³ for 8 hours/day, 5 days/week for 8.9 years resulted in decreased pulmonary function, such as decreased residual levels of maximal mid-expiratory flow rates and forced expired volume/functional vital capacity (FEV/FVC) (US EPA, 1994).

In a two-year lifetime exposure study, a LOAEL of 0.4 ppm (1.16 mg/m³) for respiratory epithelial damages was observed in rats and mice (Wolf *et al.*, 1995 as cited in OEHHA, 1997). Mice and male rats (70 animals per group) were exposed to chlorine concentrations of 0, 0.4, 1 and 2.5 ppm (0, 1.16, 2.9 or 7.25 mg/m³) for 6 hours/day, 5 days/week. On the other hand female rats were exposed to 3 days/week, as a result of the observed higher sensitivity of the female rats. Significant histological changes in respiratory epithelia were observed in female rats exposed to concentrations above the 0.4

ppm (1.16 mg/m³) level. Respiratory lesions studied included goblet cell hyperplasia, respiratory epithelium eosinophilic accumulation, glandular epithelium eosinophilic accumulation and olfactory epithelium eosinophilic accumulation.

Klonne *et al.* (1987 as cited in OEHHA, 1997) exposed 32 male and female rhesus monkeys to chlorine at concentrations of 0, 0.1, 0.5 and 2.3 ppm (approximately 0, 0.3, 1.5 and 6.7 mg/m³) for one year. The monkeys displayed statistical increases in tracheal and nasal lesions at the highest exposure, and a slight increase at the lower exposure levels.

3.3 Developmental/Reproductive Toxicity

Due to the limited information available from human and animal studies, the US Environmental Protection Agency (US EPA) has not drawn any conclusion on developmental or reproductive toxicity of chlorine (US EPA, 1994). In its derivation of its criterion for chlorine, the Massachusetts Department of Environmental Protection concluded that there was little evidence to suggest that chlorine acts as a developmental or reproductive toxicant (MDEP, 1995).

Female Sprague-Dawley rats given chlorine concentrations of 0, 1.0, 10, or 100 mg/L in their drinking water for 2.5 months prior to conception and throughout gestation, were killed on gestation day 20, and the fetuses were examined. Resorptions were not increased at any concentration. However, soft tissue defects were observed in fetuses in the 100 mg/L group, including improper orientation of the heart and adrenal agenesis, and a slightly increased incidence of skeletal variants, such as incompletely ossified or missing sternebrae or rudimentary ribs (US EPA, 1994). In other studies, pregnant mice were administered with chlorine in drinking water as 29-38 mg/m³ of sodium hypochlorite and hydrochloric acid (to maintain water pH of 2.5). Results were negative for reproductive and teratogenic effects when administered as described above, or when given in heavily chlorinated municipal drinking water (US EPA, 1994). B6C3F1 mice that were given 1.6 and 4.0 mg/kg/day of chlorine as dissociated hypochlorite (OCI) had sperm head abnormalities, however no sperm abnormalities were observed at 8.0 mg/kg or when given as hypochlorite (HOCl) (US EPA, 1994).

3.4 Genotoxicity

There are equivocal results on the mutagenicity of chlorine. It was mutagenic in *Salmonella typhimurium* strains TA1530 and TA100, without metabolic activation, produced chromosome aberrations in human lymphocytes and other mammalian cells at 1798 mg/m³, interacted with DNA in E. Coli polA test (as sodium hypochlorite), and was negative for the induction of erythrocyte micronuclei or chromosome aberrations of bone marrow cells of Swiss CD-1 mice (up to 8 mg/kg/day of NaOCI) for up to 5 days (US EPA, 1994).

3.5 Carcinogenicity

Due to limited data, the US EPA has not drawn any conclusion on the carcinogenicity of chlorine (US EPA, 1994). In a study of F344/N male and female rats, and B6C3F₁ male and female mice (50/sex/group), received 0, 70, 140, or 275 ppm (0, 203, 406 or 798 mg/m³) chlorine in their drinking water for 2 years. The results from this study showed that the female rats had a slight increase in the incidence of mononuclear cell leukemia, but it was not clearly dose-related (control, 8/50; low dose, 7/50; mid-dose, 19/51; high-dose, 16/50), however it was considered by the US National Toxicology Program (NTP) to be "equivocal evidence of carcinogenic activity" in male rats or male and female mice at the doses tested (NTP, 1992). In another study, chlorine administered as NaOCl to rats in drinking water at levels up to 1000 mg/L for males and 200 mg/L for females showed no signs of carcinogenicity. (NTP, 1992). The NTP noted that some epidemiologic studies have shown an association between the consumption of chlorinated drinking water and an increased risk for the development of cancer, primarily of the urinary tract. However, the role of molecular chlorine versus chlorination by-products, such as chloroform, is unclear (NTP, 1992).

3.6 Environmental Effects

Chlorine, although essential to plant growth, is also phytotoxic. Chlorine is absorbed by and accumulates in plant leaves. Foliar injury is dependent upon chlorine concentration and species as well as exposure duration. The most sensitive species found in the available literature are radishes and alfalfa which demonstrated a toxicity threshold for leaf damage of 0.29 mg/m³ (0.1 ppm) after a 2-hour exposure to chlorine (Brennan et al, 1965). Acute toxicity to lower plants is characterized by defoliation with no-leaf symptoms and, in higher plant forms, by spotting of the leaves (at 1.5 mg/m³) and interveinal injury at 150 to 300 mg/m³ (US EPA, 1994). Crops (bean, radish, and rose) began to show foliar injury after exposure to 3.8 mg/m³ chlorine for a half hour (Zimmerman, 1955). A study conducted on the Granary weevil showed 30% survival after exposure to 1% Cl₂ gas for 10 minutes and 38% survival after exposure to 20% Cl₂ gas for 2 minutes (Leukel, 1940).

Chlorine has high acute toxicity to aquatic organisms as many toxicity values are less than 1 mg/L. Ninety-six-hour LC₅₀ values for aquatic organisms range from 0.017 mg/L for the water flea, *Daphnia pulex* (Hall, 1981) to 0.1 mg/L for fathead minnow (*Pimephales promelas*) (Environment Canada, 1984).

4.0 Existing Air Quality Regulations

4.1 Overview

Ontario's current half-hour POI standard for chlorine is $300 \mu\text{g}/\text{m}^3$, which is based on health effects. The 24-hour AAQC is currently set at $150 \mu\text{g}/\text{m}^3$ and has been established on the basis of the health and vegetation effects (MOEE, 1994a). Chlorine was identified as a priority contaminant for review based on both its pattern of use in Ontario, and toxicological information that has been published subsequent to the development of the existing standard in 1984.

Rationale documents from the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government were reviewed for the existence and basis of air quality criteria for chlorine. A brief summary of this review is presented in Table 1 and agency-specific summaries concerning air quality guidelines for chlorine are presented in Section 11.0 of the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE normally uses a factor of 15 to convert from criteria based on annual average concentrations to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of those reviewed, 5 agencies have air guidelines (the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts). These agencies have developed their criteria from workplace exposure limits. The acute exposure limits vary between 15 and $350 \mu\text{g}/\text{m}^3$, and chronic exposure guidelines vary between 3.95 and $7.1 \mu\text{g}/\text{m}^3$. The Netherlands have an emission standard of $5,000 \mu\text{g}/\text{m}^3$. The State of California is proposing its revised criteria for chlorine: an acute reference exposure level of $210 \mu\text{g}/\text{m}^3$ and a chronic level of $0.06 \mu\text{g}/\text{m}^3$ level (OEHHA, 1997). These criteria are derived from human and animal studies. A risk assessment for chlorine is under review by the US EPA.

Table 1. Summary of Existing Air Quality Guidelines^[1] for Chlorine

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA	No ambient air exposure limits are available. RfC: under review.		1997	No air guideline promulgated.
California	Chronic REL (Reference Exposure Level): 7.1 µg/m ³ . Proposed: chronic REL, 0.06 µg/m ³ (annual average) Acute REL: 23 µg/m ³ (1-hour average) Proposed: acute REL, 210 µg/m ³ (1-hour average)	TLV-TWA from ACGIH. Respiratory effects Respiratory irritations Irritant effects.	1.99e+11	Chlorine appears on the Toxic Air Contaminants Identification List.
Massachusetts	TEL (Threshold Effects Exposure Limits): 3.95 µg/m ³ (24-hour average). AAL (Allowable Ambient Limit): 3.95 µg/m ³ (annual average).	TLV-TWA from ACGIH. TLV-TWA from ACGIH.	1995 1995	Adjusted to allow for exposures via other media. Adjusted to allow for exposures via other media.
Michigan	ITSL (Initial Threshold Screening Level): 15 µg/m ³ (8-hour average).	TLV-TWA from ACGIH.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC (Reference Concentration for Inhalation): 7.1 µg/m ³ (annual average)	Chronic REL from California	1997	Adopted California's REL. Used for permitting.
New York State	SGC (Short-term Guideline Concentration): 350 µg/m ³ (1-hour average). AGC (Annual Guideline Concentration): 3.5 µg/m ³ .	REL-TWA from NIOSH. REL-TWA from NIOSH.	1991 1991	Used for permitting. Used for permitting.
WHO	None.			
Netherlands	5,000 µg/m ³ (half-hour average).	Emission standard.	1992	Used for permitting.
Sweden	None.			
CEPA	None.			
Ontario	POI Standard: 300 µg/m ³ (half-hour). AAQC: 150 µg/m ³ (24-hour).	Health effects. Health and vegetation effects.	1984	Air quality standard.

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.

4.2 Evaluation of Existing Criteria

Due to lack of data, no agency has performed a carcinogenicity risk assessment, therefore the cancer end-point has not been considered a basis for their criteria.

The States of California, Michigan, New Jersey and New York, and the Commonwealth of Massachusetts have based their criteria, or reference exposure levels for chlorine on occupational exposure limits. Specifically, the criteria of the states of Massachusetts, Michigan and California are based on the American Conference of Governmental Industrial Hygienists' (ACGIH) limit, and that of the State of New York standard is based on the National Institute for Occupational Safety and Health's (NIOSH) limit. New Jersey has adopted the chronic reference exposure level of the State of California.

The ACGIH developed its occupational exposure limits based on health studies on workers. It was reported that exposures of 1 ppm of chlorine for 8 hours produced statistically significant changes in pulmonary function and increased subjective irritation. At lower concentrations, chlorine did not affect the lower respiratory tract but may irritate the eyes, nose and throat (ACGIH, 1991, ACGIH, 1999). The ACGIH recommended a threshold limit value-time weighted average (TLV-TWA) of 0.5 ppm (1.5 mg/m³) for chlorine to prevent eye and mucous membrane irritation, based on studies examining chlorine-induced irritations experienced by human subjects (ACGIH, 1991). NIOSH also recommended an exposure limit (REL) of 0.5 ppm (1.5 mg/m³), which is based on the consideration of eye and respiratory irritations (NIOSH, 1988).

The variation in the values of the air quality criteria of these agencies reflect slightly different science/policy considerations in the application of uncertainty factors, particularly when deriving an ambient level criterion from a workplace exposure limit. New York State applied an uncertainty factor of 4.2 to the REL of 1,500 µg/m³ of the NIOSH to come up with its short-term guideline concentration (SGC) value of 350 µg/m³. New York State also applied a factor of 420 (4.2 for exposure derivation and 100 for a "moderate toxicity" for chlorine) to the REL of NIOSH to obtain its annual guideline concentration (AGC) of 3.5 µg/m³.

The Massachusetts Department of Environmental Protection (MDEP) obtained its criterion (threshold effects exposure limit, TEL) of 3.95 µg/m³ by dividing the occupational exposure limit of 1,500 µg/m³ of the ACGIH by a total uncertainty factor of 367.5 calculated as 4.2 for extrapolation from a work week to continuous exposure, 1.75 to account for difference in sensitivity between adults and children, 10 to account for high risk groups and 5 for multimedia exposure (MDEP, 1994).

The State of Michigan applied an uncertainty factor of 100 to the TLV-TWA (1,500 µg/m³) of the ACGIH to obtain its initial threshold screening level (ITSL) of 15 µg/m³. In its derivation, the

uncertainty factor included: the conversion of discontinuous to environmental exposures with a factor of 4.2; a worker may spend half of his/her life span in the work environment (30 over 70 years); and 10 for sensitive individuals.

In deriving its current chronic exposure level, the State of California modified the previous TLV-TWA of $2,900 \mu\text{g}/\text{m}^3$ (1 ppm; 1969-1988) from the ACGIH using an uncertainty factor of 420 (4.2 to extrapolate from a 40 hour work week, 10 for extrapolating from workers to the general population, and 10 to go from a LOEL to a NOEL, as adverse effects are reported at this level).

Recently, the Office of Environmental Health Hazard Assessments of the California EPA has proposed a revised chronic inhalation reference exposure level (REL) of $0.06 \mu\text{g}/\text{m}^3$, based on a well-designed animal inhalation study (see Appendix 9.2). In this two-year lifetime exposure study, a LOAEL of 0.4 ppm ($1.16 \text{ mg}/\text{m}^3$) for respiratory epithelial damages was observed in rats and mice (Wolf *et al.*, 1995, as cited in OEHHA, 1997). It was found that a parallel analysis, using the benchmark (BM) dose analysis, performed on data for glandular epithelium eosinophilic accumulation in female rats resulted in a BMC_{05} (benchmark concentration) of 0.14 ppm ($0.4 \text{ mg}/\text{m}^3$), which was 3-fold lower than the identified LOAEL. A BMC_{05} or a BMC_{10} is considered to be similar to a NOAEL in estimating a concentration associated with a low level risk. The LOAEL was corrected for continuous exposure and extrathoracic respiratory effects. Uncertainty factors of 10 for a LOAEL instead of a NOAEL, 3 and 10 for inter- and intra-species variabilities, respectively, were then applied to obtain a proposed REL of 0.02 ppb or $0.06 \mu\text{g}/\text{m}^3$.

California identifies the strength of the REL since it is based on a well conducted inhalation study using multiple doses. Given that rhesus monkeys also exhibited similar adverse effects as rodents, California suggests that rodents are an appropriate model for humans. It also recognised that no NOAEL has been observed, there are limited reproductive data on chlorine and inadequate data on human exposure.

California is also proposing to revise its present acute reference exposure level of $23 \mu\text{g}/\text{m}^3$ to $210 \mu\text{g}/\text{m}^3$ (OEHHA, 1998). The present value was adopted from ACLs (ambient concentration limits) derived by Lewis and Alexeeff (CAPCOA, 1993). The proposed value is derived from the study of Anglen (1981 as cited in OEHHA, 1998). In this study where human volunteers were exposed, a NOEL of 1 ppm ($2,900 \mu\text{g}/\text{m}^3$) was observed for a half-hour exposure. This value was extrapolated to a one-hour exposure of $2,100 \mu\text{g}/\text{m}^3$. An uncertainty factor of 10 was then applied for extrapolation to sensitive populations to obtain an acute REL of $210 \mu\text{g}/\text{m}^3$. However, in the study of Anglen (1981), it was reported that exposure at 1 ppm ($2,900 \mu\text{g}/\text{m}^3$) for 1 hour produced consistent, and statistically significant increase in throat irritation and a significant decrease in the group's mean forced expiratory volume (FEV_1 ; possible changes in pulmonary function). Exposure to 0.5 ppm ($1,500 \mu\text{g}/\text{m}^3$) for 4

hours did not consistently induce throat irritation and urge to cough. Therefore, this may cast doubts in the determination of an appropriate NOAEL by the OEHHA (see section 11.2).

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including chlorine, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and any technical or economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received one submission from a stakeholder regarding the draft document for chlorine. A rubber manufacturer indicated that they were in the process of reducing emissions of chlorine, therefore a new standard between $30 \mu\text{g}/\text{m}^3$ and $150 \mu\text{g}/\text{m}^3$ should not present any difficulties.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholder comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for chlorine. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for Chlorine

The current AAQC (24-hour average) for chlorine is $150 \mu\text{g}/\text{m}^3$ and has been established on the basis of the health and vegetation effects. The current POI standard (half-hour average) is $300 \mu\text{g}/\text{m}^3$ and is based on the health effects of this compound.

Chlorine is a corrosive agent and an irritant to the skin, eyes and the respiratory system. Exposure by inhalation at a level above 0.5 ppm ($1,500 \mu\text{g}/\text{m}^3$) may cause irritation to the throat. Higher levels of exposure may affect the respiratory system causing tracheal and bronchial changes, emphysema, chronic pulmonary edema, and congestion as well as damage to the blood tissues.

The US EPA has not provided a health risk assessment for chlorine for exposures through inhalation. Five U.S. states have derived their respective air quality criteria from the occupational exposure limit of 0.5 ppm ($1,500 \mu\text{g}/\text{m}^3$), from the ACGIH or the NIOSH. These limits were established for the protection of workers from the irritating effects of chlorine. The State of California has established a chronic REL of $7.1 \mu\text{g}/\text{m}^3$, which is based on the adverse health effects of chlorine. The OEHHA of the California EPA has recently proposed a revised chronic inhalation REL of $0.06 \mu\text{g}/\text{m}^3$, based on a two-year (lifetime) exposure study for respiratory epithelial damages in rats and mice.

The reported geometric mean of the odour thresholds for chlorine is $232 \mu\text{g}/\text{m}^3$ which has been used to derive an odour based AAQC for chlorine.

Levels of chlorine which have been found to be toxic to plants are much higher than those considered appropriate for the protection of human health. Thus, a health-based air quality standard should also provide sufficient protection for vegetation.

8.0 Recommendations

The Ministry of the Environment has reviewed, and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed the Ministry has evaluated and accepted the rationale which supports the current occupational exposure limit of $1,500 \mu\text{g}/\text{m}^3$ (0.5 ppm) from the ACGIH. The Ministry will also review the toxicological information supporting the proposed inhalation REL of the California EPA and those comments received following the completion of the public review process for this compound to determine if MOE's POI and AAQC need to be revised.

The occupational exposure limit of $1,500 \mu\text{g}/\text{m}^3$ is divided by a factor of 1.5 to convert from an 8-hour TWA to 24-hour average concentration and an uncertainty factor of 100 is applied to obtain a 24-hour AAQC of $10 \mu\text{g}/\text{m}^3$. The Ministry of the Environment normally uses a factor of 3 to derive half-hour

POI standards and guidelines from criteria based on a 24-hour average concentrations. This factor is derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for chlorine:

- a 24-hour average AAQC of $10 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine based on the health effects of this compound; and,
- a 10-minute AAQC of $230 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine based on the odour nuisance of this compound.

Based on supporting science and dispersion modelling, a half-hour POI standard of $30 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $300 \mu\text{g}/\text{m}^3$ to this revised level of $30 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- $30 \mu\text{g}/\text{m}^3$ to $300 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chlorine.

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the

proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion

models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;

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- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>*

Comments relevant to the setting of air quality standards for chlorine can be sent to:

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NPRI, 1995. The National Pollutant Release Inventory, summary report and database of 1995. Canadian Environmental Protection Act. Environment Canada.

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NPRI, 1997. The National Pollutant Release Inventory, summary report and database of 1997. Canadian Environmental Protection Act. Environment Canada.

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources. Albany, New York.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

OEHHA, 1998. Technical Support Document for the Determination of Acute Toxicity Exposure Levels for Airborne Toxicants - Chlorine. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (TTSL, IRS�, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

US EPA, 1994. Chemical Summary for Chlorine. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC.

US EPA, 1997. Integrated Risk Information System Database. United States Environmental Protection Agency, Washington, DC.

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

Wolf, D.C., *et al.* 1995. Two year inhalation exposure of female and male B6C3F1 mice and F344rats to chlorine gas induces lesions confined to the nose. *Fund. Appl. Toxicol.* 24: 111-131. As cited in OEHHA, 1997, *op cit.*

Zimmerman, P.W. 1955. Chemicals Involved in Air Pollution and Their Effects Upon Vegetation. *Prof. Papers Boyce Thompson Inst.* 2: 124-145.

11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Chlorine (CAS# 7782-50-5)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

For threshold effects, a risk assessment for the chronic inhalation Reference Concentration (RfC) of chlorine is currently under review by the US EPA (1997). The evaluation for chlorine's human carcinogenic potential is under review by an inter-office Agency work group (US EPA, 1997). No air concentration guidelines exist for chlorine.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature, to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

No information available.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

No information available.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for chlorine. However, a risk-based chronic reference exposure level (REL) of $7.1 \mu\text{g}/\text{m}^3$ has been adopted for chlorine, based on a threshold limit value (TLV) established by the American Conference of Governmental Industrial Hygienists (ACGIH). At present, the State of California has also adopted an acute one hour REL of $23 \mu\text{g}/\text{m}^3$ for chlorine. This level is equivalent to the ambient concentration limit (ACL) which is applied in "quantitative risk assessments of non cancer health effects for acute exposure to air pollutants." This REL is currently being revised by the State and a new level for the acute one-hour REL of $210 \mu\text{g}/\text{m}^3$ is being proposed and has just been released for public comment. In addition, a new chronic reference exposure level of $0.06 \mu\text{g}/\text{m}^3$ has been proposed by this state agency for public review.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritising substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the

OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

The draft document on the Determination of Acute Toxicity Exposure Levels for Airborne Toxicants was released for public comment in 1996 (ARB, 1997). This report provides the supporting documentation rationale for the development of new acute toxicity exposure levels to be applied to various airborne toxicants. It identifies key studies, summarises the human and animal health effects of these toxicants and presents the derivation of revised acute one hour RELs which will be adopted in the future. It must be noted that this is a draft document which is still undergoing public review (OEHHA, 1998).

5. Documentation Available:

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 233-235.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels - Chlorine. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

OEHHA, 1998. Technical Support Document for the Determination of Acute Toxicity Exposure Levels for Airborne Toxicants - Chlorine. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

Key reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices, Sixth Edition. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. Peer-Review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification List is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (e.g., Hazardous Substances Database, Integrated Risk Information System, International Agency for Research on Cancer, etc.) and additional widely recognised reference texts.

The reference concentrations (RfCs), RELs, and cancer potency values reported in both the Draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required. The Determination of Acute Toxicity Exposure Levels for Airborne Toxicants has been released for public comment, and is currently undergoing public review.

7. Status of Guideline:

Not applicable

8. Key Risk Assessment Considerations:

The chronic REL of $7.1 \mu\text{g}/\text{m}^3$ is based on the ACGIH TLV-Time-Weighted-Average (TLV-TWA) of $2,900 \mu\text{g}/\text{m}^3$ (established prior to 1989), modified by an uncertainty factor of 420. This factor was derived by multiplying a factor of 4.2 (used to account for the extrapolation from a 40 hour work week to a 168 hour full week) by 10 times (to extrapolate from healthy to sensitive workers), and by another 10 times (since adverse health effects have been often reported at this TLV-TWA level). The ACGIH has since lowered the TLV-TWA for chlorine to $1,500 \mu\text{g}/\text{m}^3$. The State has acknowledged this change, and submitted a proposal to lower their REL accordingly (California Environmental Protection Agency, 1997).

Recently, the Office of Environmental Health Hazard Assessments of the California Environmental Protection Agency has proposed a revised chronic inhalation reference exposure level of $0.06 \mu\text{g}/\text{m}^3$, based on a well-designed animal inhalation study (OEHHA, 1997). This key study involved rats and mice of both sexes, large number of animals (280 per sex per species; 70 per group), a two-year lifetime exposure period, and appropriate selection of endpoints (respiratory epithelial lesions including goblet cell hyperplasia, respiratory epithelium eosinophilic accumulation, glandular epithelium eosinophilic accumulation and olfactory epithelium eosinophilic accumulation.). Mice and male rats were exposed to chlorine concentrations of 0, 0.4, 1 and 2.5 ppm (0, 1.16, 2.9 or $7.25 \text{ mg}/\text{m}^3$) for 6 hours/day, 5 days/week. The female rats were exposed to 3 days/week because the authors observed higher sensitivity of the female than the male animals. Statistically significant histological changes in respiratory epithelia were observed in female rats at and above the 0.4 ppm ($1.16 \text{ mg}/\text{m}^3$) level. Statistically significant responses were observed in the traditional and respiratory epithelial regions of all exposed rats and mice. Similarly significant damages to the olfactory epithelium occurred in all exposed rats and female mice and also in the male mice exposed to 1.0 ppm ($2.9 \text{ mg}/\text{m}^3$) and 2.5 ppm ($7.25 \text{ mg}/\text{m}^3$) concentrations. The 0.4 ppm ($1.16 \text{ mg}/\text{m}^3$) was considered the LOAEL of this study. In order to extrapolate for human exposure, the LOAEL of 0.4 ppm ($1.16 \text{ mg}/\text{m}^3$) was corrected for continuous environmental exposure (for 6 hours/day; 3 days/week) and for extrathoracic respiratory effects (for

human equivalent concentration; $RGDR=0.16$; $BW = 229 \text{ g}$; $MV = 0.17 \text{ L/min}$; $SA(ET) = 15 \text{ cm}^2$). In addition, an uncertainty factor of 300 was applied, including 10 for using a LOAEL instead of a NOAEL; 3 for inter-species variability and 10 for intra-species variabilities. Finally, a proposed chronic exposure reference level of 0.02 ppb or $0.06 \mu\text{g}/\text{m}^3$ was obtained. Performing a benchmark dose (BMC_{05}) analysis on data for glandular epithelium eosinophilic accumulation in female rats resulted in a 3-fold lower value than the LOAEL of 0.4 ppm ($1.16 \text{ mg}/\text{m}^3$). A BMC_{05} or BMC_{10} has been considered to be similar to a NOAEL in estimating a concentration associated with a low level risk.

The acute REL of $23 \mu\text{g}/\text{m}^3$ was adopted from the ACLs derived by Lewis and Alexeeff (CAPCOA, 1993). This limit is applied as a risk-based short-term one-hour exposure level for chlorine (CAPCOA, 1993). The toxicological endpoint considered in the development of both the chronic and acute REL is respiratory irritation (ARB, 1996). The proposed new acute one-hour REL of $210 \mu\text{g}/\text{m}^3$ is derived from an epidemiological study by Anglen (1981) which examined the effects of chlorine on the respiratory system. This study identified a 30-minute exposure to $2,900 \mu\text{g}/\text{m}^3$ to chlorine to be a no-observed-adverse-effects-level (NOAEL). The new REL of $210 \mu\text{g}/\text{m}^3$ was then calculated by adjusting this NOAEL with an uncertainty factor of 10 for sensitive individuals, and extrapolating to a one-hour exposure.

However, in the study of Anglen (1981), it was reported that exposure to chlorine at 1 ppm ($2,900 \mu\text{g}/\text{m}^3$) for 1 hour induced consistent and statistically significant increase in throat irritation and a significant decrease in group mean forced expiratory volume (FEV_1 ; possible changes in pulmonary function). Exposure to 0.5 ppm ($1,500 \mu\text{g}/\text{m}^3$) for 4 hours did not consistently induce throat irritation and urge to cough. There is no detail reported by the OEHHA how the exposure time of 30 minutes was determined. As well, the LOAEL would appear to be 1 ppm and the NOAEL be 0.5 ppm. A no-observed-effect level of 0.4 ppm ($1,160 \mu\text{g}/\text{m}^3$) for an 1-hour exposure had been observed for the lack of an effect on changes in FEV_1 in human volunteers with hypersensitive airways (D'Alessandro *et al.*, 1996 as cited in OEHHA, 1998).

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for chlorine. The State recognises that the US EPA's RfC is currently under review (ARB, 1996). Chlorine is not listed under Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996).

Chlorine is identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment," which is the State's next step in establishing a potential air quality guideline value (ARB, 1997).

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Chlorine is not one of these substances.

11. *Other Relevant Factors:*

Chlorine is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Chlorine (CAS# 7782-50-5)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) is $3.95 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The Allowable Ambient Limit (AAL) is $3.95 \mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts Air Quality Program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure levels, regulatory implications, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1987. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure

limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TEL and AAL where appropriate and defensible. In the case of chlorine, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH occupation exposure limit for chlorine, has adopted the level of 0.5 ppm (equivalent to 1.45 mg/m³, assuming 25°C, 1 atmosphere, and molecular weight of 70.91 g/mol). For use in the MDEP air guidelines this level was considered the Most Appropriate Occupational Limit (MAOL) and adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This converts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week to 24 hours per day, seven days per week.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 1 to account for relatively complete data in the toxicity database used to review the potential toxicity of chlorine.

The factor applied to the MAOL to calculate the "adjusted" MAOL is $4.2 \times 1.75 \times 10 = 73.5$. The adjusted MAOL is numerically equivalent to $1.45 \text{ mg/m}^3 / 73.5 = 0.1973 \text{ mg/m}^3 = 19.73 \text{ }\mu\text{g/m}^3$. At this point, another set of uncertainty factors were applied to the adjusted MAOL:

-
- I. divided by 1. This is an uncertainty factor which accounts for documented developmental or reproductive effects that chlorine exhibits (MDEP, 1990) but has been unaccounted for in the health assessment. Since there is little evidence to suggest that chlorine acts as a developmental or reproductive toxicant, the uncertainty factor is defined as 1.
 - II. divided by 5 to account for exposure through other media sources. This is based on an assumption that ambient air represents only 20% of the total exposure.

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 367.5. The TEL for chlorine was therefore calculated as $3.95 \mu\text{g}/\text{m}^3$.

Non-Threshold Effects

The MDEP reported that there was insufficient evidence to classify chlorine's carcinogenic or mutagenic potential (MDEP, 1990). The non-threshold effect exposure limit (NTEL) was developed from the adjusted MAOL ($19.73 \mu\text{g}/\text{m}^3$) using a non-threshold effects uncertainty factor (NTEUF) of 1. No adjustment was made for multimedia considerations. The resulting NTEL for chlorine was calculated as $19.73 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the TEL for chlorine of $3.95 \mu\text{g}/\text{m}^3$ was adopted as the AAL.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end-point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not include consideration of technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

The adjusted MAOL used as the basis of the guideline was divided by 5 to allow for contributions from sources of exposure other than air.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)
2. *Agency:* State of Michigan, Department of Environmental Quality (DEQ)
3. *Guideline Value(s):*
The 8-hour Initial Threshold Screening Level (ITSL) is 15 $\mu\text{g}/\text{m}^3$.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the Air Toxic Rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRSL, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices. Sixth Edition. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of this value. Specifically, the American Conference of Governmental Industrial Hygienists' (ACGIH) process for development of Threshold Limit Values (TLVs), upon which the ITSL for chlorine is based, were employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for chlorine was determined from the Threshold Limit Value-Time-Weighted-Average (TLV-TWA) established by the ACGIH and has an averaging time of 8 hours. The ITSL was determined by dividing the occupational exposure level (OEL) (in this case, the TLV-TWA from ACGIH) by 100. The 100 fold safety factor is derived as follows:

$$\begin{aligned}\text{ITSL} &= \text{OEL} \times A \times B \times C \\ &= \text{OEL} \times \frac{40 \text{ hours}}{168 \text{ hours}} (A) \times \frac{30 \text{ years}}{70 \text{ years}} (B) \times \frac{1}{100} (C) = \frac{\text{OEL}}{100}\end{aligned}$$

where:

A adjusts for the difference between a 40 hour work week and the total hours in a week;

B adjusts for the difference between the number of years a person is assumed to work and the total estimated lifetime;

C adjusts for the possible higher susceptibility of certain individuals in the general population when compared to the healthy adult worker.

The ACGIH established a TLV-TWA of 0.5 ppm for chlorine (ACGIH, 1991). TLV-TWAs refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse health effects.

With a conversion factor of $1 \text{ ppm} = 2.9 \text{ mg/m}^3$, 0.5 ppm is equivalent to 1.45 mg/m^3 or $1,450 \text{ } \mu\text{g/m}^3$. This was divided by 100 and rounded up to arrive at the ITSL of $15 \text{ } \mu\text{g/m}^3$.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)

2. *Agency:* Department of Environmental Protection (NJDEP) - State of New Jersey

3. *Guideline Value(s):*

The State of New Jersey has not identified a specific air concentration guideline value for chlorine. The New Jersey Bureau of Air Quality Evaluation (BAQEv) bases its guideline values on the information made available from the US EPA and other sources. A reference concentration (RfC) of $7.1 \mu\text{g}/\text{m}^3$, based on the reference exposure level outlined under the State of California's Committee of the California Air Pollution Control Officers Association (CAPCOA) 1993 Risk Assessment Guidelines has been adopted by the NJDEP (NJDEP, 1997).

4. *Application:*

The BAQEv Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available:*

NJDEP, 1997. Memorandum regarding the revision of Reference Concentration List. Department of Environmental Protection.

NJDEP, 1994. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

Key Reference(s):

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The State adopted the State of California's chronic REL of $7.1 \mu\text{g}/\text{m}^3$ (NJDEP, 1997). This risk-based reference level is based on the ACGIH TLV-Time-Weighted-Average (TLV-TWA) for chlorine. The derivation of this level is detailed in section 5.2 State of California.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. Unit risk factors (URFs) must be used to calculate inhalation risks for carcinogens, while potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, RfCs must be used for inhalation exposure, and reference doses (RfDs) are used for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Chlorine (CAS#7782-50-5)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources

3. *Guideline Value(s):*

Short-term Guideline Concentration (SGC) for chlorine is $350 \mu\text{g}/\text{m}^3$ (1-hour average). Annual Guideline Concentration (AGC) for chlorine is $3.5 \mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Daft. New York State Department of Environmental Conservation, Division of Air Resources. Albany, New York.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. *Key Risk Assessment Considerations:*

Chlorine is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC was derived from the NIOSH Recommended Exposure Limit-Time Weighted Average (REL-TWA) of 1.5 mg/m³ (1988) by dividing the NIOSH REL-TWA by 4.2 and rounding down to 350 µg/m³. The AGC was derived from NIOSH REL-TWA (1988) by dividing the NIOSH REL-TWA by 420 and rounding down to 3.5 µg/m³.

$$\text{SGC} = 1.5 \text{ mg/m}^3 / 4.2 = 0.357 \text{ mg/m}^3 = 350 \text{ µg/m}^3$$

$$\text{AGC} = 1.5 \text{ mg/m}^3 / 420 = 0.00357 \text{ mg/m}^3 = 3.5 \text{ µg/m}^3$$

The factor used above as the divisor to adjust the occupational limit is based on adjusting 8 hour/day, 5 days/week occupational exposure to 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2). To compensate for applying occupational guidelines to the general population in establishing an AGC, an additional factor of 10 is used for contaminants defined as low toxicity chemicals and a factor of 100 is used for contaminants defined as moderate toxicity chemicals.

9. *Key Risk Management Considerations:*

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guideline considers only human exposure to contaminants in the air.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*
None.

4. *Application:*
None.

5. *Documentation Available:*
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*
Not applicable.

7. *Status of Guideline:*
Not applicable.

8. *Key Risk Assessment Considerations:*
None.

9. *Key Risk Management Considerations:*
None.

10. *Multimedia Considerations of Guidelines:*
None.

11. *Other Relevant Factors:*
None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Chlorine is classified as a class 2 gaseous inorganic substance (gA.2). This classification imposes an emission standard of 5,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 0.05 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. *Peer-Review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 5,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 0.05 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

9. *Key Risk Management Considerations:*

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Chlorine (CAS# 7782-50-5)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

The air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority, called the National Licensing Board for Environmental Protection. The basis for the guidelines is permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

Key Reference(s):

None available.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1,000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} .

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Chlorine (CAS # 7782-50-5)
2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*
3. *Guideline Value(s):*

No guideline has been established. Chlorine has not been assessed or evaluated under the first Priority Substance List (PSL1). It was nominated as a substance for consideration, but was not recommended for evaluation by the Ministers' Expert Advisory Panel under the Second Priority Substance List (PSL2).

Application:

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
CHLOROFORM**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Chloroform was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1979. A review of the scientific and technical information relevant to setting ambient air quality standards for chloroform has previously been provided to stakeholders for their comments. This document therefore provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for chloroform.

Chloroform, CAS # 67-66-3, is a colourless and very volatile liquid with a characteristic odour and a burning sweet taste. Chloroform is used as a grain fumigant and as a solvent for pesticides, adhesives, fats, oils, rubbers, alkaloids, and waxes. It is also a chemical intermediate for dyes and pesticides and is a component of cough syrups, toothpastes, and liniments. Chloroform is used in fire extinguishers to lower the freezing temperature of carbon tetrachloride. It is also used in the manufacturing of fluorocarbon refrigerants, propellants, plastics, anaesthetics, and pharmaceuticals.

Data obtained from Environment Canada's National Pollutant Release Inventory (NPRI) summary report indicates that less than 0.5 tonnes of chloroform was released annually to air across Canada in 1993 and 1994. The releases of chloroform in Canada soared to 234.45 tonnes in 1995, and showed a small decline to 215.4 tonnes in 1997. No reportable quantity of chloroform was released in Ontario in 1993 and 1994. Reported releases in Ontario jumped to about 44 tonnes in 1995. The reported releases in 1996 and 1997 were 36.7 and 56 tonnes, respectively. Of the 1997 releases in Ontario, more than 98% was attributed to air emissions. The pulp and paper mill products industries accounted for most of the releases in 1995 to 1997. Based on estimates of mean exposures from various media, the general population is exposed to chloroform primarily in food, drinking-water and indoor air.

Chloroform is well absorbed in animals and humans when exposed through ingestion, inhalation, and dermal contact. In humans, 60-80 % of inhaled chloroform is absorbed, and is distributed throughout the entire body. The tissue distribution is dependent on exposure route. Extrahepatic tissues receive a higher dose from inhaled or dermally absorbed chloroform than from ingested chloroform. Metabolism of chloroform involves cytochrome P-450 in an oxidative biotransformation to produce trichloromethanol, with phosgene as its intermediate product and finally to hydrochloric acid and carbon dioxide. Chloroform can also undergo a reductive biotransformation to produce the dichloromethyl radical. Both phosgene and dichloromethyl radical can form covalent adducts. Unmetabolized chloroform is retained in fat longer than in any other tissue.

Chloroform is a central nervous system depressant and a gastrointestinal irritant. It has caused rapid death due to cardiac arrest. Exposure to chloroform can cause fainting, vomiting, dizziness, salivation, nausea, fatigue, and headache. Other symptoms may include respiratory depression, coma, and kidney and liver damage. Of these, the most universally observed toxic effect of chloroform is liver damage. Chronic exposure to chloroform can result in loss of appetite, hallucinations, moodiness, and physical and mental sluggishness. Occupational effects have included lassitude, thirst, gastrointestinal distress, frequent and scalding urination, lack of concentration, depression, irritability, staggering, hepatitis, and jaundice. Chloroform can be toxic to the embryos or fetus and affect reproduction, but is not teratogenic. The weight-of-evidence from a large number of sensitive assays suggests that neither chloroform nor its metabolites appear to possess genotoxic activity. The carcinogenic data in humans is limited. However, there is sufficient evidence to suggest that chloroform is an animal carcinogen.

A carcinogenic risk assessment for chloroform has been carried out by the United States Environmental Protection Agency (US EPA). The US EPA Carcinogen Assessment Group's (CAG) quantitative risk assessment for chloroform is based on data from an NCI cancer bioassay in which there was a statistically significant increase in hepatocellular carcinomas in male and female mice, and renal epithelial tumours in male rats fed with chloroform by gavage. Currently there are inadequate data to assess human carcinogenicity. There are no available epidemiological studies which indicate that chloroform was the sole chemical agent that cohort populations were exposed. Based on sufficient carcinogenicity evidence in animals, various agencies have classified chloroform as a probable or possible human carcinogen. These agencies include the US EPA, the International Agency for Research on Cancer (IARC), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Institute for Occupational Safety and Health (NIOSH), the American National Toxicology Program (NTP) and the Occupational Safety and Health Administration (OSHA).

The current Ontario air quality guideline and criterion for chloroform were established in 1979. The half-hour POI guideline is $1,500 \mu\text{g}/\text{m}^3$ and the 24-hour AAQC is $500 \mu\text{g}/\text{m}^3$. These criteria were established on the basis of health effects.

In revising the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Of these agencies, the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, and the Netherlands have considered both the carcinogenic and non-carcinogenic endpoints in their air quality guideline development. California has recently proposed a non-cancer acute Reference Exposure Level of $360 \mu\text{g}/\text{m}^3$ and a chronic REL of $300 \mu\text{g}/\text{m}^3$.

The US EPA has developed an Inhalation Unit Risk (IUR) of $2.3 \times 10^{-5} \cdot (\mu\text{g}/\text{m}^3)^{-1}$ for chloroform based on tumour incidence in mice. This IUR corresponds to an air concentration of $0.4 \mu\text{g}/\text{m}^3$ for an excess lifetime cancer risk of 1 in 100,000, or $0.04 \mu\text{g}/\text{m}^3$ for an excess lifetime cancer risk of 1 in 1,000,000. Using data additional to those of the US EPA, the State of California estimated the risk-specific concentration to be $0.19 \mu\text{g}/\text{m}^3$ at an excess lifetime cancer risk of 1 in 1,000,000. The World Health Organisation (WHO), however considers chloroform a threshold carcinogen. From oral studies in mice the WHO derived a Tolerable Daily Intake of $10 \mu\text{g}/\text{kg}$ body weight or approximately $35 \mu\text{g}/\text{m}^3$ to protect from the cancer effects of chloroform. In view of the information reviewed from leading agencies and the assessment of toxicological profile (carcinogenic effects) for chloroform, the Ministry has decided to derive air quality standards for this compound based on the rationale for the risk estimate from the State of California.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for chloroform:

- **an annual average AAQC of $0.2 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chloroform based on the carcinogenic effect of this compound; and,**
- **a 24-hour average AAQC of $1.0 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chloroform based on the carcinogenic effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $3 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $1500 \mu\text{g}/\text{m}^3$ to this revised level of $3 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$3 \mu\text{g}/\text{m}^3$ to $300 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chloroform; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process

will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Chloroform was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing guideline in 1979. A review of scientific and technical information relevant to setting an ambient air quality standard for chloroform had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for chloroform.

2.0 General Information

2.1 Physical and Chemical Properties

The following table provides some general information on chloroform and its properties:

CAS #	67-66-3
RTECS #	FS9100000
UN #	1888
Conversion Factors	1 ppm = 4.9 mg/m ³ 1 mg/m ³ = 0.204 ppm @ 25°C and 101.3 kPa
Boiling Point	61.7 °C
Flash Point	Nonflammable
Henry's Law Constant	314.1 Pa m ³ /mol at 20°C
Log K _{OW}	1.97
Formula	CHCl ₃
Molecular Weight	119.39 g/mol
Vapour Density (air = 1)	4.12
Vapour Pressure	100 mm @ 10.4 °C
Common Synonyms	Trichloromethane, formyl trichloride, Freon 20, methane trichloride

Chloroform is a clear, colourless, and very volatile liquid with a characteristic odour and a burning sweet taste. Odour thresholds of 133-276 ppm (652-1352 mg/m³) with a geometric mean of 192 ppm (940 mg/m³) have been reported (AIHA, 1989). Pure chloroform is light-sensitive, requiring reagent grade chloroform to be stabilised with 0.75% ethanol (WHO, 1994).

2.2 Uses

Chloroform is used as a grain fumigant and a solvent for pesticides, adhesives, fats, oils, rubbers, alkaloids, and waxes. It is also a chemical intermediate for dyes and pesticides and is a component of cough syrups, toothpastes, and liniments (US EPA, 1994). Chloroform is used in fire extinguishers to lower the freezing temperature of carbon tetrachloride (Windholz *et al.*, 1976). It is also used in the manufacturing of fluorocarbon refrigerants, propellants, plastics, anaesthetics, and pharmaceuticals (ACGIH, 1991; WHO, 1994).

2.3 Sources and Levels

Sources

Chloroform is a naturally-occurring compound, however human activity is responsible for most of the chloroform found in the environment (ATSDR, 1997). Chloroform is one of several substances formed by the reaction of chlorine, in water disinfected with chlorine, with organic matter. It is also produced as a result of pulp and paper operations where chlorine is used for bleaching purposes (WHO, 1994). It is also produced industrially (for what purpose(s)).

Environment Canada's National Pollutant Release Inventory (NPRI) summarises the emissions of chemicals in Canada based on information provided by reporting facilities. Data obtained from the NPRI reports indicate that less than 0.5 tonnes of chloroform was released, annually to air, across Canada in 1993 and 1994. Atmospheric releases of chloroform were 0.013 and 0.039 tonnes in 1993 and 1994, respectively. Reported releases increased dramatically to 234.45 tonnes in 1995 (as a result of 9 sources) and showed a small decline to 215.4 tonnes in 1997 (as a result of 8 sources). Atmospheric emissions of chloroform in Ontario showed a similar pattern, but at a much smaller scale than national releases. In 1993 and 1994, the reported atmospheric releases in Ontario were far below the reporting criteria. The most significant increase occurred in 1995, about 44.4 tonnes (from 1 reporting facility) were released. The releases in Ontario in 1996 and 1997 were 36.7 and 56 tonnes, respectively (from 2 and 3 reporting facilities, respectively). 1997 NPRI report indicated that more than 98 % of the releases in Ontario were attributed to air emissions. The pulp and paper mill products industries accounted for most of the releases in these past years.

Ambient Air Concentrations

Environment Canada has collected ambient air data for chloroform levels from January 1993 to December 1995 from thirty-nine monitoring stations across Canada. From 4,233 samples, a mean concentration of $0.16 \pm 0.11 \mu\text{g}/\text{m}^3$ was observed for chloroform. The concentrations reported ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $3.39 \mu\text{g}/\text{m}^3$ (Environment Canada, 1997).

Results from air sampling surveys between 1988 - 1992 in the Windsor area, in Ontario indicated that chloroform was detected at low levels however, 50% of the time chloroform was not detected. Most of the 24-hour average chloroform concentrations were less than $1.0 \mu\text{g}/\text{m}^3$. The maximum concentrations ranged from $0.32 - 1.9 \mu\text{g}/\text{m}^3$ (MOEE, 1994b). Half-hour average monitoring data collected down-wind from a few hazardous waste and landfill sites, in Ontario during 1994 and 1995 indicated chloroform levels ranged from 0.01 to $4.4 \mu\text{g}/\text{m}^3$ (MOEE, 1997).

In order to determine the median Ground Level Concentration a sample of 25 Certificates of Approval, of sources that emit Chloroform, were reviewed by the Ministry. As a result the median Ground Level Concentration, estimated by dispersion modelling in Regulation 346 for all 25 sources was approximately $30.4 \mu\text{g}/\text{m}^3$. The maximum and minimum were 895 and $0.10 \mu\text{g}/\text{m}^3$, respectively.

Based on estimates of mean exposures from various media, the general population is exposed to chloroform primarily in food, drinking-water and indoor air. The estimated intake from outdoor air is considerably less than in food, drinking water or indoor air. Data suggest that chlorinated water use in homes contributes considerably to levels of chloroform in indoor air and in total exposure, with total intakes up to $10 \mu\text{g}/\text{kg}$ body weight per day (WHO, 1994).

2.4 Environmental Fate

Due to its volatility, most chloroform is emitted to air. In water, chloroform is transferred to air, where it has a residence time of several months (WHO, 1994). Chloroform can, therefore, be transported over long distances from its source. Atmospheric degradation of chloroform with hydroxy radicals may occur and this process has an estimated half-life of around 60 days. In the presence of chlorine, irradiation of chloroform may lead to the formation of hydroxy radicals. Hydroxy radicals may then react with chloroform to form intermediate products which may react with oxygen to form phosgene in the atmosphere (WHO, 1994). Biodegradation in soils by aerobic and anaerobic microbial populations is limited, however, chloroform is toxic to these microorganisms at high concentrations (ATSDR, 1997). Chloroform does not appreciably bioconcentrate in freshwater fish based upon measured bioconcentration factors of 6 to 8 for bluegill sunfish and 14 for fathead minnows (ATSDR, 1997).

3.0 Toxicology of Chloroform

The following toxicological review of chloroform is primarily focussed on the inhalation route of exposure as this is the predominant pathway of human exposure and that most of the released chloroform is emitted to the air. Data on other exposure media are included where relevant or where inhalation data are lacking. Both oral and inhalation routes of exposure effect the liver and kidney (OEHHA, 1997a).

Chloroform is well absorbed by animals and humans when exposed through ingestion, inhalation, and dermal contact. Studies in humans indicated that 60-80% of inhaled chloroform is absorbed. The exposure concentration and species-specific metabolic capacities determine the absorption kinetics of chloroform following inhalation (WHO, 1994). Once absorbed, chloroform distributes throughout the entire body. Tissue distribution is dependent on exposure route. Extrahepatic tissues receive a higher dose from inhaled or dermally absorbed chloroform than from ingested chloroform. Highest tissue

levels are reached in the fat, blood, liver, kidneys, lungs, and nervous system. Placental transfer of chloroform has been demonstrated in humans and several species of animals (WHO, 1994).

Metabolism of chloroform involves an oxidative biotransformation (favoured at low chloroform concentrations, e.g. <0.1 mM) by cytochrome P-450 to produce trichloromethanol or a reductive biotransformation (at high substrate concentrations) to produce the dichloromethyl radical. Through the oxidative pathway, the loss of hydrochloric acid from chloroform results in the formation of phosgene as an intermediate, which reacts rapidly with water to generate hydrochloric acid and carbon dioxide. Phosgene may react with nucleophiles or macromolecules to form covalent adducts. Cell damage and death have been suggested as the result of the reaction of phosgene with tissue proteins. The dichloromethyl radical may bind to phospholipids to form covalent products. The balance of the oxidative and reductive metabolic pathways depends on factors such as oxygen and chloroform concentrations, animal species, strain, enzyme induction and the site of metabolism. Unmetabolized chloroform is retained in fat longer than in any other tissue (WHO, 1994).

In humans and animals exposed to chloroform, carbon dioxide and unchanged chloroform are eliminated in the expired air. The fraction of the dose which is eliminated as carbon dioxide is dependent on the dose and the species. The rate is slower in human hepatic and renal microsomes than in rodent hepatic and renal microsomes (WHO, 1994). Chloroform has been ranked 11 on the list of 275 priority hazardous substances under the U.S. Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) for detailed risk assessments.

3.1 Acute Toxicity

Chloroform is a central nervous system depressant and a gastrointestinal irritant. It has also been reported to cause rapid death due to cardiac arrest. Exposure to chloroform can cause fainting, vomiting, dizziness, salivation, nausea, fatigue, and headache. Other symptoms may include respiratory depression, coma, and kidney and liver damage (US EPA, 1994). Of these, the most universally observed toxic effect of chloroform is liver damage. In animal studies, chloroform-induced death through the oral route of exposure is mostly attributable to liver damage. Certain strains of mice may be genetically more susceptible to chloroform-induced acute toxicity. Sex-related difference in acute chloroform toxicity in the kidney has been observed in male mice (such an effect is not observed in female mice). Death from kidney damage due to inhalation exposure has been observed in male C3H mice between 3400 to 5400 mg/m³ (WHO, 1994). An LC₅₀ (lethal concentration; 50% killed) of 6150 mg/m³ (6 hours exposure) has been reported in OF1 female mice. Non-lethal liver toxicity was observed in mice and rats at chloroform levels of 490 and 1410 mg/m³, respectively, after a single 4-hour inhalation exposure (WHO, 1994). Kidney tubules degeneration has been reported in rabbits through dermal exposure up to 4 g/kg body weight for 24 hours.

3.2 Subchronic/Chronic Toxicity

Chronic exposure to chloroform can result in loss of appetite, hallucinations, moodiness, and physical and mental sluggishness (US EPA, 1997). In an occupational setting, four full-time and four half-time workers, mostly female, in a factory manufacturing lozenges, with chloroform were exposed to average chloroform concentrations of 375 to 1,330 mg/m³ (with a peak concentration of 5,680 mg/m³) for periods of 3 to 10 years (WHO, 1994). Symptoms reported included lassitude, thirst, gastrointestinal distress, frequent and scalding urination, lack of concentration, depression and irritability. In addition, some of these employees had been observed staggering. Nine other workers, of which only one was full-time, suffered to a lesser degree from the same conditions noted above after exposure to 110 to 350 mg/m³ of chloroform for 10 to 24 months (WHO, 1994). A higher frequency of hepatitis was found for 68 workers exposed to chloroform at the work place, than in the general inhabitants of the city in which the factory was located. The workers were exposed to concentrations of 10 to 1,000 mg/m³ for 1 to 4 years (WHO, 1994). Chloroform also caused toxic jaundice in 13 workers who were exposed to more than 1,950 mg/m³ of chloroform for under 6 months, and in 18 workers who were exposed to 80 to 160 mg/m³ for less than 4 months (WHO, 1994).

Male Wistar rats (36 per group) exposed to chloroform continuously at 245 mg/m³ for 4 weeks or at 1387 mg/m³ for 6 hours/day, 5 days/week for 4 weeks, total exposure for the two methods was 154 g/m³-hours, resulted in various degrees of liver injuries. The severity was related to the exposure patterns: liver injuries were more severe by continuous exposure than by repeated exposures (WHO, 1994). Rats (10 - 12 of each sex per group) were exposed to chloroform at 0, 110, 230 and 410 mg/m³ for 7 hours/day, 5 days/week for 6 months. Kidney weight increases in animals, in both sex groups were observed in all dose groups. Histological changes in the kidneys and livers of male rats were more prominent at higher doses, these changes were reversible after the cessation of the treatment at 110 mg/m³. Death of some males occurred at the 410 mg/m³ dose due to interstitial pneumonitis.

3.3 Developmental/Reproductive Toxicity

Chloroform can be embryo- or fetotoxic and effect reproduction, but is not teratogenic (WHO, 1994). Fetuses of Sprague-Dawley rats exposed to chloroform concentrations of 147, 490 and 1,470 mg/m³ for 7 hours/day during days 6-15 of gestation showed growth retardation and minor skeletal aberrations (delayed ossification of skull and sternebrae) (WHO, 1994). Groups of 35-40 pregnant CF₁ mice were exposed to 0 and 490 mg/m³ for 7 hours/day throughout days 1-7, 6-15, or 8-15 of gestation. The ability of females to maintain pregnancy was significantly decreased after exposure to chloroform during day 1-7 or 6-15 of gestation, fetuses from these groups had significantly decreased mean fetal body weight and crown-rump length (WHO, 1994). Delayed ossification of skull bones and sternebrae was observed in fetuses from all exposed groups, especially days 1-7 and 8-15 exposed groups. The

incidence of cleft palates significantly increased in fetuses from females exposed to 490 mg/m³ during days 8-15 of gestation (WHO, 1994).

3.4 Genotoxicity

In Ames assays with bacteria *Salmonella typhimurium* or *Escherichia coli*, with and without metabolic activation, and conducted under sealed conditions for the volatility of chloroform, in three separate studies most of the results reported were negative (WHO, 1994). There was only one study providing positive results, with an uncommon test using *Photobacterium phosphorum*. No mutagenic activity was observed in the majority of the studies with non-mammalian eukaryotic systems (yeasts and fungi) and two sex-linked recessive lethal tests with *Drosophila melanogaster*. Negative results were also obtained in DNA repair assays and micronucleus tests (WHO, 1994). Chloroform did induce sister-chromatid exchange in two separate *in vitro* studies using hamster ovary cells or human lymphocytes, without metabolic activation, and in a mice study using an *in vivo* system with bone marrow cells. Chloroform has been submitted to a large number of sensitive genotoxicity assays, resulting in few positive responses, which were randomly distributed among the various assays with no apparent pattern or clustering for any particular test system. The resulting weight-of-evidence evaluation suggests that chloroform does not possess genotoxic activity (WHO, 1994).

3.5 Carcinogenicity

Chloroform has been associated with the development of cancer because of its presence as a predominant trihalomethane in chlorinated drinking water, and since it is known as a animal carcinogen (ATSDR, 1997). However, such an association cannot be adequately supported in epidemiological studies with chlorinated drinking water because of the existence of many confounding factors such as, co-existence of other trihalomethanes and other potential carcinogenic compounds produced during the chlorination of drinking water, the non-specificity of the cancer types observed, the history of exposure to chlorinated drinking water and other chemicals, and the lack of data in chloroform concentrations in these studies. There are no studies available regarding the carcinogenicity of chloroform in humans, or animals by the inhalation route of exposure. Most of the cancer data were obtained from animal studies in which chloroform was given through the oral route of exposure, e.g. in drinking water, food or by gavage (WHO, 1994; ATSDR, 1997). The following provides a brief summary for some of these studies.

Short-term oral exposure studies did not provide consistent results. Chloroform given to mice in oil by gavage at a dose of 594 mg/kg/day for 30 days had an increased incidence of hepatomas. In another study, chloroform given to mice in oil by gavage at a dose of 1800 mg/kg/day for 8 weeks did not induce lung tumours in these animals. No increase in tumours was observed in mice exposed to chloroform in drinking water at 257 mg/kg/day for 52 weeks (ATSDR, 1997).

Chloroform was found to be carcinogenic in several long-term oral animal studies. Chloroform given to mice and rats in corn oil by gavage induced liver and kidney tumours. Renal tubular cell adenoma and carcinoma were noticed in male Osborne-Mendel rats following a 78-week (5 days/week) exposure to chloroform at 90 mg/kg/day by gavage in corn oil. In contrast, no increase in tumour incidences was observed in Sprague-Dawley rats exposed to chloroform in toothpaste by gavage at 60 and 165 mg/kg/day for 80 and 50 weeks, respectively. (ATSDR, 1997).

In a National Cancer Institute (NCI) study, B6C3F₁ mice were given chloroform in corn oil by gavage for 78 weeks (5 days/week), the animals were sacrificed for tumour analysis after a total of 92 weeks. The dose levels were adjusted after 18 weeks, resulting in time-weighted average doses of 138 (low dose) and 277 (high dose) mg/kg for male mice and 238 (low dose) and 477 (high dose) mg/kg for female mice. At the highest administered dose, death in some animals occurred. Causes of death may be attributed to treatment-related liver tumours, pulmonary inflammation and cardiac thrombosis. The incidence of chloroform-induced hepatocellular carcinoma in male mice was: 1/18, 18/50 and 44/45 at 0, 138 and 277 mg/kg, respectively; in female mice, it was: 0/20, 36/45 and 39/41 at 0, 238 and 477 mg/kg, respectively.

In the same NCI study, Osborne-Mendel rats were given chloroform in corn oil by gavage five times a week for 78 weeks and the animals were sacrificed after 111 weeks. The dose levels were adjusted after 23 weeks, resulting in time-weighted average doses of 90 (low dose) and 180 (high dose) mg/kg for male rats and 100 (low dose) and 200 (high dose) mg/kg for female rats. At all the administered doses, reduced survival in male and female animals occurred. The pathological reason for the death was unknown. The incidence of chloroform-induced kidney epithelial tumours for male rats was: 0/19, 4/50 and 12/50 at 0, 90 and 180 mg/kg, respectively. In female rats, the incidence for non-significant increases in thyroid tumours was: 1/19, 8/49 and 10/46 at 0, 100 and 200 mg/kg, respectively. In an independent study, in which the NCI experiments were re-evaluated, the same neoplastic lesions were observed in rats. In addition, chloroform-treated female rats developed a higher incidence of liver tumours (cholangiofibromas, cholangiocarcinomas and hepatocellular carcinomas) which were not seen in controls (WHO, 1994).

3.6 Environmental Effects

Information pertaining to the effects of chloroform on terrestrial wildlife is not available.

Seven-day LC₅₀ values for amphibians range from 0.3 mg/L for the frog, spring creeper, (*Hyla crucifer*) to 35 mg/L for the toad (*Bufo fowleri*); the no-observed-lethal concentrations (NOLC) range from 0.009 to 0.33 mg/L (WHO, 1994).

Ninety-six-hour LC_{50} values for several fish species range from 18 mg/L for rainbow trout (*Salmo gairdneri*) (Anderson et al, 1980) to 171 mg/L for fathead minnow (*Pimphales promelas*) (Mayes et al, 1983), NOLC values range from 3 mg/L for bluegill sunfish (*Leopomis macrochirus*) to 8 mg/L rainbow trout (Anderson et al, 1980).

The effects of chronic exposures (27 days) of fish embryo and larval stages to chloroform have been studied for rainbow trout; a 96-hour LC_{50} of 2.0 mg/L was determined for hatching (Birge et al., 1979). Larval death was observed at concentrations of 10.6 mg/L. The frequency of teratogenesis in a hatched population previously exposed to 0.056 mg/L chloroform was 3%, but the frequency of teratogenesis increased to 40% at chloroform concentrations of 10 mg/L. Chloroform is moderately toxic to the water flea, *Daphnia magna* (48-hour LC_{50} = 29 mg/L) (LeBlanc et al, 1980).

Chloroform is of low toxicity to unicellular plants and other microorganisms. The concentration range of initial population growth inhibition was in the range of 125 mg/L to >3,200 mg/L (WHO, 1994).

4.0 Existing Air Quality Criteria

4.1 Overview

The current Ontario air quality guideline and criterion for chloroform was established in 1979 on the basis of health effects. The half-hour POI guideline is 1,500 $\mu\text{g}/\text{m}^3$ and the 24-hour AAQC is 500 $\mu\text{g}/\text{m}^3$ (MOEE, 1994a).

The documentation for ten agencies (the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government) was reviewed for the existence and basis of air quality criteria for chloroform. A brief summary of this review is presented in Table 1 and agency-specific summaries of information concerning air quality guidelines for chloroform are presented in the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria based on annual average concentrations to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994c). However,

Table 1. Summary of Existing Air Quality Guidelines^[1] for Chloroform

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA	No ambient air exposure limits are available.			
	0.4 µg/m ³ for excess lifetime cancer risk of 1 in 100,000. 0.04 µg/m ³ for excess lifetime cancer risk of 1 in 1,000,000. RfC (Reference Concentration): under review.	Tumour incidence in female mice.	1987	IUR: $2.3 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$. IUR may not be appropriate at concentrations exceeding 400 µg/m ³ .
California	1.9 µg/m ³ for lifetime cancer risk of 1 in 100,000.	Arithmetic mean of unit risks generated by several studies.	1993	IUR: $5.3 \times 10^{-4} (\mu\text{g}/\text{m}^3)^{-1}$. The conversion from the RfD assumes equal absorption occurs by the oral and inhalation routes. OEHHA proposed revision OEHHA proposed revision
	0.19 µg/m ³ for lifetime cancer risk of 1 in 1,000,000.			
	Chronic REL (Reference Exposure Level): 35 µg/m ³ .	US EPA RfD (Oral Reference Dose).		
	Proposed chronic inhalation REL: 300 µg/m ³ . Proposed acute inhalation REL: 360 µg/m ³ (1-hour).	Liver, kidney and developmental effects Bony proliferation in nasal passage		
Massachusetts	TEL (Threshold Effects Exposure Limits): 132.76 µg/m ³ (24-hour average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 0.04 µg/m ³ (annual average).	IUR from US EPA (IRIS).	1995	Excess lifetime cancer risk of 1 in 1,000,000 implied by the level adopted from US EPA.
Michigan	IRSL (Initial Risk Screening Level): 0.4 µg/m ³ with an annual averaging time. SRSL (Secondary Risk Screening Level): 4.0 µg/m ³ lifetime excess cancer risk of 1 in 100,000.	Derived from the geometric mean of two cancer potency studies reporting kidney tumours in rats. Lifetime excess cancer risk of 1 in 1,000,000.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
New Jersey	URF (Unit Risk Factor): $2.3 \times 10^{-3} (\mu\text{g}/\text{m}^3)^{-1}$.	IUR from US EPA (IRIS).	1994	Permitting application. The URF must be used to assess cancer risks in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): $980 \mu\text{g}/\text{m}^3$ (1-hour average).	STEL from NIOSH.	1991	Used for permitting
	AGC (Annual Guideline Concentration): $0.04 \mu\text{g}/\text{m}^3$ ^[3] .	IUR from US EPA (IRIS).	1991	Excess lifetime cancer risk of 1 in 1,000,000 implied by the level adopted from US EPA.
WHO	None.			
Netherlands	$20,000 \mu\text{g}/\text{m}^3$ (half-hour average).	Emission standard.	1994	Used for permitting.
	National MIC (Maximum Immissible Concentration): $7.5 \mu\text{g}/\text{m}^3$ (annual average).	Province of Groningen's guideline.		Target value: $1 \mu\text{g}/\text{m}^3$ (annual average).
Sweden	None.			
CEPA	None.			
Ontario	half-hour POI guideline: $1,500 \mu\text{g}/\text{m}^3$.	Both the POI and AAQC are based on health.	1994	POI guideline
	24-hour AAQC: $500 \mu\text{g}/\text{m}^3$.			

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.
- In the process of reviewing the New York State Air Guidelines, the Department of Environmental Conservation indicated that the air guidelines were derived from a reference concentration (RfC) reported in the US EPA's IRIS database (NYSDEC, 1997a). However, a review of IRIS revealed that no RfC was available for chloroform. The agency was contacted for further clarification on the derivation of the SGC and AGC. At that time, the agency reported that the current AGC was adopted from the carcinogenic risk assessment conducted in IRIS. The summary here reflects the correct value for the AGC. The SGC is still current. (NYSDEC, 1997b).

depending on the health end-point being considered, other conversion factors may also be employed.

Of those reviewed, the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, and the Netherlands, have developed criteria which were based on the carcinogenic and /or non-carcinogenic effects of chloroform.

The US EPA has developed an Inhalation Unit Risk (IUR)¹ for chloroform of $2.3 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ based on liver tumour incidence in female mice (US EPA, 1997). The US EPA's inhalation Reference Concentration (RfC) for chloroform is under review.

The IUR of the California agency was derived from the arithmetic mean of unit risks for kidney tumors generated by several studies. California also has a chronic Reference Exposure Level based on the Oral Reference Dose (RfD) developed by the US EPA. Recently, the Office of Environmental Health Hazard Assessment (OEHHA, 1997a) of the California Environmental Protection Agency (California EPA) has proposed a revised chronic REL of $300 \mu\text{g}/\text{m}^3$ for chloroform, based on the liver and kidney effects of this compound and an acute (1-hour) REL of $360 \mu\text{g}/\text{m}^3$ base on effects on the nasal passage in rats (OEHHA, 1998).

The State agencies of New York, New Jersey and the Commonwealth of Massachusetts have derived their cancer-based criteria from the US EPA's IUR. The agency of Michigan has established its IUR from the geometric mean of IUR from two kidney tumour studies. In addition to cancer-based IUR, the agencies of New York and Massachusetts have also developed non-cancer-based criteria. The Short-term Guideline Concentration for New York is based on the National Institute of Occupational Safety and Health's (NIOSH) Short-Term Exposure Limit (STEL) of 2 ppm ($9.8 \text{ mg}/\text{m}^3$) which is based on the lowest level that could be reliably measured. The Threshold Effects Exposure Limit for Massachusetts is based on the ACGIH's Threshold Limit Value-Time-Weighted Average (TLV-TWA) of 10 ppm ($49 \text{ mg}/\text{m}^3$) which is based on the protection of workers against liver and kidney cancer and necrosis, cardiac arrhythmias, central nervous system depression and fetal toxicity (ACGIH, 1991). The agency of Massachusetts also makes use of an additional consideration for multimedia exposure in the derivation of the Threshold Effects Exposure Limit.

The Netherlands have three criteria, an emission standard used in permitting, a Maximum Immissible (sic) Concentration (an annual average) adopted from a provincial guideline, and a Target Value, which is not an enforceable standard but an eventual goal for ambient levels. The WHO, Sweden or the Canadian Federal government do not have air quality guidelines for chloroform. Chloroform has been

¹For the purposes of this review, the term Inhalation Unit Risk, as defined by the US EPA, will be used and abbreviated as IUR. IUR describes the same concept as Unit Risk Factor (URF) or Unit Risk Estimate (URE). URF and URE will be employed where specific agencies use them in their criteria documents.

identified in the Priority Substance List (PSL) 2 for assessment under the *Canadian Environmental Protection Act* (CEPA) (Environment Canada, 1995). This assessment will determine the level of exposure in Canada and determine whether chloroform is "toxic" as defined under Section 11 of CEPA.

4.2 Evaluation of Existing Criteria

The regulation of long-term exposure to chloroform is based on two approaches: those based on avoidance of injury to the central nervous system, liver and kidneys and those based on the avoidance of cancer in the liver or kidneys. The two approaches will be examined separately in the following sections.

Criteria Based on a Carcinogenicity End-Point

The available carcinogenicity-based criteria for chloroform have been derived from animal tumourigenic studies, in which chloroform was given orally. Available epidemiological studies on chloroform carcinogenicity do not provide reliable data for cancer risk assessment because of the confounding factors in those studies (section 3.5). In the Integrated Risk Information System (IRIS) database of the US EPA, chloroform is classified as a probable human carcinogen (Classification B2) (US EPA, 1997). The International Agency for Research on Cancer (IARC) has classified chloroform as a possible human carcinogen (Group 2B) which is based on evidence of carcinogenicity in animals and limited evidence of carcinogenicity in humans (IARC, 1987). These classifications are accepted by the American agencies which have established criteria for chloroform, i.e., California, Massachusetts, Michigan, New York and New Jersey. Furthermore, the American Conference of Governmental Industrial Hygienists (ACGIH) classifies chloroform as a suspected human carcinogen (A2 carcinogen). In the U.S.A., both the National Institute for Occupational Safety and Health (NIOSH) and the Occupational Safety and Health Administration (OSHA) rate chloroform as a carcinogen. The American National Toxicology Program (NTP) classifies chloroform as "reasonably anticipated to be a carcinogen" (Group 2) (ACGIH, 1991).

The inhalation quantitative risk assessment conducted by the US EPA is based on data from the National Cancer Institute study (US EPA, 1997; NCI, 1976). In the NCI study, chloroform was administered by gavage to male and female B6C3F₁ mice for five times a week for 78 weeks. The time-weighted average dosages were 138 and 277 mg/kg for male mice and 238 and 477 mg/kg for female mice. There were 20 animals per sex in the control group and 50 animals per sex in each dose group. Significant dose-related increases in the incidence of hepatocellular carcinomas were reported for both male and female mice (see section 3.5 for tumour incidences). Male mice that did not develop hepatocellular carcinomas were observed to have a high incidence of liver nodular hyperplasia. Extrapolation of metabolism-dependent carcinogenic dose-responses from mice to humans was based

on body surface area, and a linearized multistage procedure was utilized to obtain the low-dose potency estimates. The tumour incidence data for male and female mice were used to derive slope factors of $3.3 \times 10^{-2} \text{ (mg/kg/day)}^{-1}$ and $2.0 \times 10^{-1} \text{ per (mg/kg/day)}$ respectively. The inhalation unit risk (IUR) of $2.3 \times 10^{-5} \text{ per } (\mu\text{g/m}^3)$ was derived by taking a geometric mean of the slope factors and assuming 100% absorption for low doses of chloroform from air.

The IRIS summary does not explicitly define the level of confidence in the risk estimates for non-threshold effects (carcinogenicity) by the inhalation exposure. However, it does cite other studies that are supportive of the risk estimates (NCI, 1976; Roe *et al.*, 1979). The US EPA last updated the carcinogenic summary for chloroform in March, 1991. New York, Massachusetts and New Jersey based their criteria on the US EPA inhalation unit risk factor (URF).

Michigan based its URF on the geometric mean of the URFs, which were calculated based the on the data from NCI (1976) and Jorgenson *et al.* (1985). Jorgenson *et al.* (1985) administered chloroform in drinking water to male Osborne-Mendel rats and female B6C3F₁ mice at concentrations of 200, 400, 900 and 1,800 mg/L for 104 weeks. These concentrations were reported to correspond to 19, 38, 81 and 160 mg/kg/day for rats and 34, 65, 130 and 263 mg/kg/day for mice. A significant increase in renal tumours in rats was observed in the highest dose group, the increase was dose related. The liver tumour incidence in female mice was not significantly increased. This study was specifically designed to measure the effects of low doses of chloroform. The data in Jorgenson *et al.* (1985) was used by the US EPA to derive the oral cancer potency of $6.1 \times 10^{-3} \text{ (mg/kg/day)}^{-1}$ (US EPA, 1997). Michigan converted this value to $1.1 \times 10^{-6} \text{ (}\mu\text{g/m}^3\text{)}^{-1}$ by assuming that the average person weighs 70 kg, breathes 20 m³/day and that chloroform is absorbed with an inhalation efficiency of 65% (MDNR, 1991).

Michigan identifies the use of the NCI (1976) study by the US EPA as the basis for the inhalation cancer risk assessment and the Jorgenson *et al.* (1985) study as the basis for the oral cancer risk assessment as an area of controversy with respect to which study is more appropriate for airborne contaminant risk assessment (MDNR, 1991). The hepatocellular carcinoma data for mice in the NCI study were excluded because the information provided to the Michigan Department of Natural Resources (MDNR) raised concerns that these tumours may be vehicle dependent (in this case corn oil) (MDNR, 1991). Renal tumour incidence was increased in both studies. The MDNR decided to use a mean potency value from the renal tumour data of the two studies. Using the URF of $6.1 \times 10^{-3} \text{ (mg/kg/d)}^{-1}$ derived by the US EPA from the Jorgenson *et al.* (1985) study, and the URF of $2.6 \times 10^{-2} \text{ (mg/kg/d)}^{-1}$ based on renal tumours from the NCI (1976) study (as derived by the State of California) Michigan established a URF of $1.3 \times 10^{-2} \text{ (mg/kg/d)}^{-1}$ or $2.4 \times 10^{-6} \text{ (}\mu\text{g/m}^3\text{)}^{-1}$, which is the geometric mean of the two URFs. This URF results in a 1 in 1,000,000 excess lifetime cancer risk concentration of $0.4 \mu\text{g/m}^3$ (MDNR, 1991).

The studies which California used to estimate the carcinogenic potency of chloroform were NCI (1976) (excluding hepatocellular carcinomas in mice) and Jorgenson *et al.* (1985) on renal tumours in male rats, Roe *et al.* (1979) on renal tumours in male mice, Tumasonis *et al.* (1985) on adenofibrosis (cholangiocarcinoma) data in female rats and Bogen *et al.* (1989) which modelled the metabolised dose of all the above bioassay studies (ARB, 1990c). California's estimate of unit risk was based on the arithmetic mean of three unit risks derived from:

1. Jorgenson *et al.* (1985);
2. NCI (1976);
3. The California Department of Health Services (CDHS)-calculated geometric mean of the Roe *et al.* (1979) and Tumasonis *et al.* (1985) studies.

The CDHS calculated a geometric mean for the Roe *et al.* (1979) and Tumasonis *et al.* (1985) studies to take into account the large number of studies indicating positive tumour response, but to de-emphasize their importance to the overall best estimate since each individual study was not as well designed as either the Jorgenson *et al.* (1985) or the NCI (1976) study.

Oral-to-inhalation extrapolation was addressed using a physiologically-based pharmacokinetic model described in Bogen *et al.* (1989), which predicted an estimate of the metabolised dose of chloroform received by a test subject. The potency estimates generated in this study were corrected for absorption of administered inhaled dose. A correction factor of 0.662 was used, which incorporated the pharmacokinetic information regarding the fraction of inhaled chloroform absorbed at low levels of exposure, as well as the fraction of inspired volume reaching the alveoli. Using estimates of cancer potency based on both administered and metabolised doses, the best estimate of the cancer unit risk from lifetime exposures to 1 ppb of chloroform in the air is 2.6×10^{-5} (or 5.3×10^{-6} per $\mu\text{g}/\text{m}^3$). Applying the inhalation unit risk (IUR) of 5.3×10^{-6} per ($\mu\text{g}/\text{m}^3$) to a population-based lifetime cancer risk of one-in-one million results in a risk-specific concentration of $0.19 \mu\text{g}/\text{m}^3$.

Most of the cancer risk estimates from the agencies described above were obtained using the linearized multistage model. This model is based on the consideration that the quantal type of biological response observed in mutagenesis and in carcinogenesis, may exhibit linear non-threshold dose-response characteristics. Chloroform has been studied for its ability to promote the formation of tumours, however results of these studies have been mixed. In a 24-week study, chloroform, at maximum tolerated dose (MTD; 1800 mg/L) or at 1/3 of MTD (600 mg/L), given in drinking water to B6C3F1 mice pretreated with diethylnitrosamine for 4 weeks developed focal necrosis in liver and kidney. Interestingly, chloroform treatment was found to decrease significantly the diethylnitrosamine-initiated lung tumours in animals (see ARB, 1990c). Chloroform did not appear to promote diethylnitrosamine-initiated tumour formation in liver and lungs of CD-1 Swiss mice. Chloroform, at a dose of 1800 ppm (mg/L) given to 15-day old mice in drinking water until the animals were 51-week of age, did not

promote ethylnitrosourea-initiated liver tumours in male mice (ethylnitrosourea did not initiate tumour formation in female mice). In fact, chloroform decreased significantly the ethylnitrosourea-initiated liver tumours in male mice (see ARB, 1990c). The studies on the role of chloroform as a tumour promoter did not provide consistent results and will require further investigations (ARB, 1990c).

In its 1994 review (WHO, 1994), the International Programme on Chemical Safety (IPCS) concluded that the carcinogenic effects of chloroform should also be considered in the development of limits of exposure. It considered a threshold effect for cell proliferation in mouse liver tumours. Based on a NOEL of 10 mg/kg body weight per day, over three weeks (Larson *et al.* 1994, as cited in WHO, 1994) it derived a tolerable daily intake (TDI) of 10 $\mu\text{g/kg}$ body weight a day (or about 35 $\mu\text{g/m}^3$, assuming a 70 kg person breathes 20 m^3 of air per day, that absorption occurs to the same extent by both routes, and toxicological effects are the same). The uncertainty factor of 1000 was used (10 for inter species extrapolation, 10 for intraspecies variation and 10 for severity of effects and less than chronic study). This compares with a 10^{-5} risk estimate using the Global 82 linearized multistage model of 8.2 $\mu\text{g/kg}$ body weight (or 29 $\mu\text{g/m}^3$) using data on induction of renal tumours in male rats (Jorgensen, *et al.*, 1985, as cited in WHO, 1994).

Criteria Based on Non-carcinogenic End-Points

The California reference exposure level (REL) of 35 $\mu\text{g/m}^3$ was derived using the US EPA's oral reference dose (RfD) of 10 $\mu\text{g/kg/day}$ established from a study on the formation of fatty cysts in the liver of beagle dogs. The REL was calculated by modifying the RfD, which is based on the oral route of exposure, to the inhalation route by assuming a 70 kg person breathes 20 m^3 of air per day, and that absorption occurs to the same extent by both routes. Recently, the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (California EPA) has proposed a revised chronic REL of 300 $\mu\text{g/m}^3$ for chloroform, based on effects in liver and kidney (OEHHA, 1997a). No NOAEL was observed in the study used (Torkelson *et al.*, 1976 as cited in OEHHA, 1997a). The REL was derived from a LOAEL of 25 ppm observed in rats exposed for six months at 0, 25, 50 and 85 ppm (123, 245, 417 mg/m^3). This was converted to a continuous dose and adjusted to a human equivalent concentration of 15.9 ppm (78 mg/m^3). An uncertainty factor of 300 was used (10 for a LOAEL was used, 3 for interspecies variations, and 10 for variations among humans).

The proposed short-term or acute REL of 360 $\mu\text{g/m}^3$ of the California EPA was derived from a study in rats (Mery, *et al.* as cited in OEHHA, 1998). Rats were exposed for 6 hours per day for seven days at 1, 3, 10, 30, 100 or 300 ppm (5, 15, 50, 150, 500 or 1500 mg/m^3). No adverse effects were noted in animals exposed to 3 ppm and lower. At 10 ppm and higher, concentration- dependent bony proliferation cellular growth in the nasal passage was observed. Using a NOAEL of 3 ppm (15 mg/m^3), the California EPA derived a 1-hour exposure equivalent dose of 7.3 ppm (36 mg/m^3) and

applied an uncertainty factor of 100 (10 for interspecies variability, and 10 for variability among humans) to obtain an acute REL of 0.073 ppm or 360 $\mu\text{g}/\text{m}^3$. This criterion can be supported by data from a developmental study. The California EPA has derived a concentration of 390 $\mu\text{g}/\text{m}^3$ as a level protective against severe acute adverse effects based on the fetotoxicity of chloroform in rats as reported in the study of Schwetz *et al.* (1974, as cited in, OEHHA 1998).

Both the agencies of New York and Massachusetts have developed a Short-term Guideline Concentration and a Threshold Effects Exposure Limit, respectively, based on occupational exposure limits. The New York's SGC of 980 $\mu\text{g}/\text{m}^3$ was derived by dividing the STEL of NIOSH by 10. The NIOSH-STEL was reported as 2 ppm (9.80 mg/m^3) (NIOSH, 1988). Under the 1991 New York State Air Guide - 1, the NIOSH-STEL was considered a ceiling limit. Therefore, the SGC for chloroform was derived differently (using a factor of 10) from most other substances (usually an occupational limit is adjusted by 4.2 to account for continuous exposure).

The Massachusetts Department of Environmental Protection (MDEP) adopted the ACGIH TLV-TWA of 10 ppm (49 mg/m^3) for chloroform as its air guideline, considering this occupational exposure limit as the Most Appropriate Occupational Limit (MAOL). The total uncertainty factor applied to the TLV-TWA value was 367.5, including a factor of 5 to account for exposure through media other than air. The resulting TEL was calculated to be 132.76 $\mu\text{g}/\text{m}^3$.

The Netherlands have developed a target value for chloroform of 1 $\mu\text{g}/\text{m}^3$ as a yearly average. This value is derived from the toxicological limit value of 100 $\mu\text{g}/\text{m}^3$ advised in the criteria document for chloroform (1985). This level was based on a study with rats, in which no effects on the liver or kidneys were found after exposure to 110 mg/m^3 for four hours a day, five days a week during six months and applying a safety factor of 1000 (a factor of 100 for differences in susceptibility between species and individuals, and a factor of 10 for discontinuous exposure). The Netherlands does not consider it appropriate to use a non-threshold approach for the calculation of a limit value for chloroform in air (Directorate-General for Environmental Protection, 1997). The MIC of 7.5 $\mu\text{g}/\text{m}^3$ for chloroform was adopted from the Province of Groningen's guideline. No additional documentation for the basis of this guideline is available in English.

The IPCS recommends a tolerable daily intake of 15 $\mu\text{g}/\text{kg}$ per day (or approximately 52.5 $\mu\text{g}/\text{m}^3$, assuming a 70 kg person breathes 20 m^3 of air per day, that absorption occurs to the same extent by both routes, and toxicological effects are the same) for protection against non-cancer effects of chloroform (WHO, 1994). This was based on toxic effects of the liver, in dogs exposed to 15 mg/kg over 7.5 years (Heywood, *et al.*, 1979, as cited in WHO, 1994). An uncertainty factor of 1000 was used (10 for variation among species, 10 for variation of sensitivity among humans, and 10 for the use a LOAEL).

5.0 Responses of Stakeholders to the Information Draft

In January, 1999, the Ministry posted information draft documents for eighteen chemicals, including chloroform, for air quality standards development under the Standards Plan (MOEE, 1996; MOE, 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agency guidelines which the Ministry considers appropriate for the development of air quality standards; the appropriateness of considering the carcinogenicity of chloroform as the most sensitive endpoint; and any technical and economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

The Ministry received one submission during the consultation period. This submission, from the utility sector, focussed primarily on the extremely low levels of stack chloroform emissions. A utility stakeholder indicated that a revised lower standard may not have significant impact on their operation.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholder comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which gave stakeholders the opportunity to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for chloroform. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for Chloroform

The current Ontario half-hour POI guideline is $1,500 \mu\text{g}/\text{m}^3$ and the 24-hour Ambient Air Quality Criterion is $500 \mu\text{g}/\text{m}^3$. These air quality guidelines were established in 1979 on the basis of the health effects of chloroform.

Chloroform is a central nervous system depressant and a systemic toxicant to the liver and kidney. Studies in animals also suggest that chloroform may be toxic to the growing foetus. California has recently proposed a non-cancer acute REL of $360 \mu\text{g}/\text{m}^3$ and a chronic REL of $300 \mu\text{g}/\text{m}^3$.

There is sufficient evidence to suggest that chloroform is an animal carcinogen. Since studies concerning inhalation exposures were not available, the six U.S. agencies reviewed have derived their air quality criteria from animal studies based on oral exposures. A clear link between human exposure and cancer has not been established, therefore, some degree of uncertainty exists in the risk estimates for humans.

The US EPA has developed an Inhalation Unit Risk of $2.3 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ for chloroform based on tumour incidence in mice. This IUR corresponds to an air concentration of $0.4 \mu\text{g}/\text{m}^3$ for an excess lifetime cancer risk of 1 in 100,000, or $0.04 \mu\text{g}/\text{m}^3$ for an excess lifetime cancer risk of 1 in 1,000,000. However, The WHO considers chloroform a threshold carcinogen. From oral studies in mice, the WHO derived a Tolerable Daily Intake of $10 \mu\text{g}/\text{kg}$ body weight or approximately $35 \mu\text{g}/\text{m}^3$ to protect from the cancer effects of chloroform. California used the arithmetic mean of three unit risks to establish an estimated risk specific concentration of $0.19 \mu\text{g}/\text{m}^3$, at an excess lifetime cancer risk of 1 in 1,000,000. The carcinogenic risk estimate obtained by the State of California considered results from multiple studies to minimize the discrepancies in experimental designs, as well as taking into account the various tumour types induced by chloroform treatment. Furthermore, California used physiologically based-pharmacokinetic models to extrapolate data from oral studies to inhalation exposures to minimize dosimetric errors in exposure route conversions. Therefore, the risk assessment performed by this agency is used in the derivation of air quality standards for Ontario.

There are insufficient data to assess the effects of chloroform on terrestrial species based on atmospheric exposures. However, based on the low cancer risk-specific concentrations derived from the risk estimate provided by the State of California, adverse effects on plants or other terrestrial organisms are not likely to occur.

The reported odour threshold of chloroform ranges from a low of $650 \mu\text{g}/\text{m}^3$ to a high of $1350 \mu\text{g}/\text{m}^3$. Odour is therefore not the limiting factor for setting air quality standards.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide and the science upon which they base their standards. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepts the scientific rationale and risk assessments which support the development of the lifetime cancer unit risk estimates of the United States Environmental Protection Agency, and the States of Michigan and California. After reviewing additional toxicological information the Ministry has decided to derive air quality standards for chloroform based on the rationale for the risk estimate from the State of California.

The Ministry strives to manage exposure to carcinogens down to a risk represented by no more than 1 excess cancer in 1,000,000. This is consistent with the Ministry's approach to carcinogenic risk management for other environmental exposures (e.g., drinking water and contaminated sites) and with other jurisdictions, in particular throughout the United States. As a result, the Ministry proposes to derive an annual AAQC based on the risk specific concentration of $0.19 \mu\text{g}/\text{m}^3$.

The Ministry of the Environment normally uses a factor of 15 to derive half-hour POI standards and guidelines from criteria based on annual average concentrations and a factor of 5 to derive 24-hour AAQC from criteria based on annual average concentrations. These factors are derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for chloroform:

- **an annual average AAQC of $0.2 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chloroform based on the carcinogenic effect of this compound; and,**
- **a 24-hour average AAQC of $1.0 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for chloroform based on the carcinogenic effect of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $3 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of $1500 \mu\text{g}/\text{m}^3$ to this revised level of $3 \mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

-
- **3 µg/m³ to 300 µg/m³ (micrograms per cubic metre of air) for chloroform; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10⁻⁶) over a lifetime up to 1 excess cancer in a population of 10,000 (10⁻⁴) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes

-
- timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry

would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for chloroform can be sent to:

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NYSDEC, 1997a. Personal communication: Mr. Thomas Gentile, New York State Department of Environmental Conservation. February 5, 1997).

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OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Chloroform. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California.

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State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Chloroform (CAS# 67-66-3)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

A chronic inhalation Reference Concentration (RfC) for chloroform is under review by an Agency work group. For carcinogenic endpoints, the Inhalation Unit Risk (IUR) for chloroform is $2.3 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$. This corresponds to a lifetime exposure air concentration of $0.4 \mu\text{g}/\text{m}^3$ for an additional cancer risk of 1 in 100,000 (10^{-5}), and a lifetime exposure air concentration of $0.04 \mu\text{g}/\text{m}^3$ for an additional cancer risk of 1 in 1,000,000 (10^{-6}). No ambient air concentration guidelines are available.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

Key Reference(s):

NCI, 1976. Report on carcinogenesis bioassay of chloroform. Report No. (NIH) 76-1279. PB-264 018. National Cancer Institute. Bethesda, Maryland.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

In the case of chloroform, the health assessment document received extensive Agency and external review (US EPA, 1997).

7. *Status of Guideline:*

No air concentration guideline exists.

8. Key Risk Assessment Considerations:

A carcinogenic risk assessment for chloroform has been carried out by the US EPA. In the IRIS database, chloroform is reported to be a probable human carcinogen (Classification B2). This classification is based on the formation of tumours in rats and three strains of mice which have been exposed to chloroform. Currently, there are inadequate data to assess human carcinogenicity. There are no available epidemiologic studies that are based solely on chloroform as the chemical agent to which cohort populations are exposed.

The inhalation quantitative risk estimate by the US EPA is based on data from a study in which chloroform was administered orally (US EPA, 1997). The US EPA used a study by the National Cancer Institute (NCI, 1976) in which chloroform in corn oil was administered by gavage to male and female B6C3F₁ mice for five days per week for 78 weeks. There were 20 animals per sex in the control group and 50 animals per sex in each dose group. The time-weighted average dosages were 238 and 477 mg/kg/day for female mice and 138 and 277 mg/kg/day for male mice. Significant dose-related increases in the incidence of hepatocellular carcinomas were reported for both male and female mice. Male mice not developing hepatocellular carcinomas were observed to have liver nodular hyperplasia. Extrapolation of metabolism-dependent carcinogenic responses from mice to humans was based on body surface area and a linearized multistage procedure was utilized to calculate the inhalation unit risk estimate. Based on the incidence data for both male and female mice, the slope factors of $3.3 \times 10^{-2} \text{ (mg/kg)}^{-1}/\text{day}$ and $2.0 \times 10^{-1} \text{ (mg/kg)}^{-1}/\text{day}$, respectively, were derived. The IUR of $2.3 \times 10^{-5} \text{ (}\mu\text{g/m}^3\text{)}^{-1}$ was derived by taking a geometric mean of the slope factors and assuming 100% absorption for low doses of chloroform in air.

The IRIS summary does not explicitly define the level of confidence in the risk estimates for non-threshold effects (carcinogenicity) by inhalation exposure. However, it does cite other studies that are supportive of the risk estimates. The US EPA last updated the carcinogenic summary for chloroform in March, 1991.

9. Key Risk Management Considerations:

The IUR should not be applied in situations where the air concentration exceeds $400 \mu\text{g/m}^3$. The IUR may not be appropriate above this concentration.

10. Multimedia Considerations of Guidelines:

No adjustment for multimedia exposure is considered in the development exposure concentrations for threshold effects or unit risk values for non-threshold effects.

11. Other Relevant Factors:

The US EPA Office of Drinking Water (ODW) used another study (Jorgenson *et al.* (1985)) upon which to base the oral cancer potency for chloroform instead of the NCI (1976) study which the US EPA's Office of Research and Development (ORD) used to base the inhalation cancer risk value. This

has created some controversy regarding which study is the most appropriate to base the cancer potency calculations. Concerns regarding the NCI (1976) study include the vehicle in which the chloroform was administered (the NCI (1976) study used corn oil, whereas Jorgenson *et al.* (1985) used drinking water) and whether the hepatocarcinomas may be vehicle related.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)

2. *Agency:* State of California: California Environmental Protection Agency (California EPA); Office of Environmental Health Hazard Assessment (OEHHA); Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for chloroform. However, a recommended inhalation unit risk estimate (IUR) of $5.3 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$, has been derived for chloroform based on carcinogenic effects in rodents. In addition, a chronic non-cancer reference exposure level (REL) of $35 \mu\text{g}/\text{m}^3$ has been adopted by the State, based on the United States Environmental Protection Agency's (US EPA's) Integrated Risk Information System (IRIS). This reference level is based on the oral reference dose (RfD) established for the chronic toxicity of chloroform in beagle dogs. Recently, the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (California EPA) has proposed a revised chronic REL of $300 \mu\text{g}/\text{m}^3$ for chloroform, based on the liver and kidney effects of this compound (OEHHA, 1997a).

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the

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- OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

The Proposed Identification of Chloroform documents were compiled as a result of a "needs assessment" as well as a response to public inquiries and prioritisation of risk assessments of the 244 substances identified under the Toxic Air Contaminants Identification List. These documents summarise the exposure and health assessments of chloroform following an extensive review of the literature by the California Department of Health Services. They are to be used as guidance reference documents for understanding the rationale behind the development of any risk-based limit value for chloroform.

5. Documentation Available:

ARB, 1990a. Proposed Identification of Chloroform as a Toxic Air Contaminant - Staff Report / Executive Summary. California Environmental Protection Agency - Air Resources Board.

ARB, 1990b. Proposed Identification of Chloroform as a Toxic Air Contaminant - Part A: Exposure Assessment. California Environmental Protection Agency - Air Resources Board.

ARB, 1990c. Proposed Identification of Chloroform as a Toxic Air Contaminant - Part B: Health Assessment. California Environmental Protection Agency - Air Resources Board.

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ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 257-261.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992-Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

Key References:

Bogen, K.T., L.C. Hall, and T.E. McKone, 1989. Draft - Health risk assessment of chloroform in drinking water. Report Number UCRL - 21170. Environmental Sciences Division, Lawrence Livermore National Laboratory, Livermore, CA.

Jorgenson, T.A., E.F. Meierhenry, C.J. Rushbrook, R.J. Bull, and M. Robinson, 1985. Carcinogenicity of chloroform in drinking water to male Osborne-Mendel rats and female B6C3F1 mice. *Fund. Appl. Toxicol.* 5: 760-769.

Mery, S., et al. 1994. Nasal toxicity of chloroform in male F-344 rats and B6C3F₁ mice following a 1 week inhalation exposure. *Toxicol. Appl. Pharmacol.* 125: 214-227.

NCI, 1976. National Cancer Institute. Report on carcinogenesis bioassay of chloroform. National Cancer Institute Carcinogenesis Program. Bethesda, MD.

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Schwetz B., *et al.* 1974. Embryo- and fetotoxicity of inhaled chloroform in rats. *Toxicol Appl. Pharmacol.* 28: 442-451.

Tumasonis, C.F., D.N. McMartin, B. Bush, 1985. Lifetime toxicity of chloroform and bromodichloromethane when administered over a lifetime in rats. *Ecotoxicol. Environ. Safety.* 9: 233-240.

6. *Peer-Review Process and Public Consultation:*

The Draft Toxic Air Contaminant Identification List is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS, IARC etc.) and additional widely recognised reference texts.

The RfCs, Reference Exposure Levels (RELs) and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines is subjected to review by the local district and the OEHHA. In addition, public input plays a

key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

The Proposed Identification of Chloroform documents were reviewed internally by staff of the Air Resources Board and were released for public comment. The answers to public concerns are addressed in Part C of the collective documents.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

The State of California accepts the IARC and US EPA classification of chloroform as a probable human carcinogen based on evidence for carcinogenicity in animals, but inadequate epidemiological data. As such, assessments conducted under the CAPCOA risk assessment guidelines must analyse the cancer risks associated with facilities emitting chloroform into the atmosphere. Compounds which must be evaluated for cancer risks are listed in Tables III-6 and Table III-7 in the CAPCOA guidelines. The cancer risks developed under these guidelines are consistent with the California EPA/OEHHA Guidelines for Chemical Carcinogen Risk Assessments and Their Scientific Rationale. Cancer risks are presented as individual excess cancer risks for inhalation pathways and are calculated by multiplying the estimated ambient air concentration at a given receptor by the chemical-specific unit risk factor. In addition, population-wide health risks posed by a facility must also be assessed as the total population excess cancer burden. This is an estimate of the increased number of cancer cases in a population as a result of exposure to an emitted substance(s).

California EPA's accepted IUR for chloroform was calculated using a linearized multistage model GLOBAL86. This model uses bioassay data to compute maximum likelihood estimates and upper 95% confidence limits of risk associated with a particular dose. The model makes several assumptions about the process of carcinogenesis, outlined below:

1. Cancer is an irreversible process which originates in a single cell with implications or involvement with a number of different biological events and/or stages.
2. The rate of occurrence of each different stage varies linearly with dose.
3. The incidences of background and chemically induced cancers are additive.

The studies which were used to estimate the carcinogenic potency of chloroform were NCI (1976) and Jorgenson *et al.* (1985) on renal tumours in male rats, Roe *et al.* (1979) on renal tumours in male mice, Tumasonis *et al.* (1985) on adenofibrosis (cholangiocarcinoma) data in female rats, and Bogen *et al.* (1989) which modelled the metabolised dose of all the above bioassay studies. Animal to human extrapolation was addressed by dose scaling on a surface area basis, and individual animal potency factors from each bioassay were corrected for by the California EPA. Therefore, human potency

factors ranged from 4.2×10^{-3} to 2.6×10^{-1} (mg/kg/day)⁻¹. California's estimate of unit risk was based on the arithmetic mean of the Jorgenson *et al.* (1985), NCI (1976) and the California Department of Health Services (CDHS) calculated geometric mean of the Roe *et al.* (1979) and Tumasonis *et al.* (1985) studies. Oral to inhalation extrapolation was addressed using a physiologically based pharmacokinetic model developed by Bogen *et al.* (1989) which predicted an estimate of the metabolised dose of chloroform received by a test subject. The potency estimates generated in this study were corrected for absorption of administered inhaled dose. A correction factor of 0.662 was used which incorporated the pharmacokinetic information regarding the fraction of inhaled chloroform absorbed at low levels of exposure, as well as the fraction of inspired volume reaching the alveoli. Applying an inhalation unit risk of 5.3×10^{-6} (µg/m³)⁻¹ to a population-based lifetime cancer risk of one-in-one million results in a risk-specific concentration of 0.19 µg/m³.

The REL of 35 µg/m³ was derived using the US EPA's oral RfD of 10 µg/m³ established from a study on the formation of fatty cysts in the liver of beagle dogs. The REL was calculated by modifying the RfD, which is based on the oral route of exposure, to the inhalation route by assuming a 70 kg person breathes 20 m³ of air per day, and that absorption occurs to the same extent by both routes.

Recently, the OEHHA has proposed a revised chronic REL of 300 µg/m³ for chloroform, based on the liver and kidney effects of this compound (OEHHA, 1997a). Rats (12/sex/group), rabbits (2-3/sex/group) and guinea pigs (8-12/sex/group) were exposed to chloroform vapour at 0, 25, 50 and 85 ppm (0, 122.5, 245 and 416.5 mg/m³) for 7 hours/day, 5 days/week for 6 months. Dogs were exposed to 25 ppm (122.5 mg/m³) chloroform for the same exposure schedule. Concentration and species-dependent pathological changes in the liver of both sexes of all animals studied included mild to severe centrilobular granular degeneration, foamy vacuolization, focal necrosis and fibrosis. Guinea pigs appeared to be the least sensitive and male rats were the most sensitive to chloroform-induced hepatotoxicity (at 122.5 mg/m³). Adverse kidney effects observed in all species included cloudy swelling of the renal tubular epithelium and interstitial and tubular nephritis. Pneumonitis was noticed in the 416.5 mg/m³ exposure groups of male rats, female guinea pigs and male rabbits, and in the 122.5 dose group of female rabbits. No NOAEL was obtained in this study. A LOAEL of 25 ppm (122.5 mg/m³) was established for the liver and kidney effects of chloroform. A chronic REL of 0.05 ppm (300 µg/m³) was derived after the adjustment for a continuous exposure period, the application of a factor 3 for animal to human gas:respiration conversion and a total uncertainty factor of 300 to the LOAEL of 25 ppm (122.5 mg/m³).

Based on acute inhalation data in rats (Mery, *et al.*, 1994) an acute (1-hour) REL has been proposed. In this study rats were exposed at 1, 3, 10, 30, 100, or 300 ppm chloroform for 6 hours per day for 7 days. Bony proliferation in the nasal passages were observed. A NOEL of 3 ppm (15mg/m³) was established. Using this NOAEL, a one hour equivalent concentration of 7.3 ppm was calculated. An uncertainty factor of 10 for interspecies extrapolation and another factor of 10 for variability within species were used to derive an acute REL of 0.073 ppm or 360 µg/m³. Using data on developmental

effects from the study by Schwetz, *et al.* (1974), 0.079 ppm (390 $\mu\text{g}/\text{m}^3$) was also calculated as being protective of severe adverse effects.

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has set a daily intake value of 20 $\mu\text{g}/\text{day}$ (oral) and 40 $\mu\text{g}/\text{day}$ (inhalation) for chloroform. Under the Safe Drinking Water and Toxic Enforcement Act, chloroform is considered a chemical known to the State to cause cancer (OEHHA, 1997b). Chloroform is rated as a probable carcinogen with a recommended inhalation IUR of $5.3 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$. Therefore, the upper 95% confidence level of the excess cancer risk for a person exposed over a lifetime to 1 $\mu\text{g}/\text{m}^3$ is estimated to be 5.3 in a million (ARB, 1996). Since chloroform is not confirmed to be a human carcinogen, the true risk may be as low as zero. The California EPA also acknowledges the US EPA has developed an IUR of $2.3 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ for chloroform, and that the US EPA's RfC for chloroform is currently under review, but does not adopt these numbers in their guidelines (ARB, 1996). Chloroform was not identified under this Proposition as a reproductive or developmental toxicant (ARB, 1996).

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Chloroform is not one of these substances.

11. *Other Relevant Factors:*

Chloroform is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program. Annual average concentrations of chloroform must also be measured, calculated and/or reported by the State, as well as any facility posting emissions, in order to be used in the analysis of cancer risk and/or chronic non-cancer effects.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Chloroform (CAS# 67-66-3)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) is $132.76 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The allowable ambient limit (AAL) is $0.04 \mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1987. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

NCI, 1976. Report on carcinogenesis bioassay of chloroform. Report No. (NIH) 76-1279. PB-264 018. National Cancer Institute. Bethesda, Maryland.

US EPA, 1985. Health assessment document for chloroform. EPA/600/8-84/004F. United States Environmental Protection Agency (US EPA), Office of Research and Development (ORD), Office of Health and Environmental Assessment, Washington, DC.

6. Peer-Review Process and Public Consultation:

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of chloroform, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH Threshold Limit Value - Time Weighted Average (TLV-TWA) occupational exposure limit for chloroform, has adopted the level of 10 ppm (equivalent to 48.8 mg/m³, assuming 25°C, 1 atmosphere, and molecular weight of 119.38 g/mol). For use in the MDEP air guidelines, this level was considered the Most Appropriate Occupational Limit (MAOL) and was adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8-hours per day, 5 days per week, to consider continuous exposure.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.

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- IV. divided by 1 to account for relatively complete data in the toxicity database used to review the potential toxicity of chloroform.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, $4.2 \times 1.75 \times 10 \times 1 = 73.5$. The adjusted MAOL is numerically equivalent to $48.8 \text{ mg/m}^3 / 73.5 = 0.664 \text{ mg/m}^3 = 664 \text{ } \mu\text{g/m}^3$. At this point, another set of uncertainty factors were applied to the adjusted MAOL:

- I. divided by 1. This is an uncertainty factor which accounts for documented developmental or reproductive effects that chloroform exhibits as teratogenic toxicant (MDEP, 1990) but which, as yet, have been unaccounted for in the health assessment. There is some evidence to suggest that chloroform acts as a moderate embryo or fetal toxicant, the uncertainty factor is defined as 1.
- II. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 367.5. The TEL was, therefore, calculated as $132.76 \text{ } \mu\text{g/m}^3$.

Non-Threshold Effects

The MDEP reported that there was sufficient evidence to classify chloroform as a probable carcinogen and sufficient evidence indicating chloroform's mutagenic potential (MDEP, 1990). The non-threshold effect exposure limit (NTEL) was developed from the cancer unit risk estimate of $2.35 \times 10^{-5} (\text{ } \mu\text{g/m}^3)^{-1}$ derived by the US EPA (1985). Using an incremental cancer risk level of one in 1,000,000 (10^{-6}), the resulting NTEL is $0.04 \text{ } \mu\text{g/m}^3$. No non-threshold effects uncertainty factor (NTEUF) or adjustment for multimedia considerations was made.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the NTEL for chloroform of $0.04 \text{ } \mu\text{g/m}^3$ was adopted as the AAL.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. *Multimedia Considerations of Guidelines:*

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. *Other Relevant Factors:*

The study (NCI, 1976) used to develop the cancer URF employed a gavage exposure route. The MDEP assumed that for gavage exposure, there are no route-specific effects on carcinogenicity potency. The MDEP also assumed that since the carcinogenic potency was based on a gavage study, it could be used to derive unit risks for other routes of exposure.

The NCI-derived URE assumes that at low air concentrations, 100% of inhaled chloroform is absorbed. The MDEP points out that this assumption may overestimate the true absorption of chloroform, which is a partially soluble gas.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)

2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)

3. *Guideline Value(s):*

The Initial Risk Screening Level (IRSL) is $0.4 \mu\text{g}/\text{m}^3$, with an annual averaging time, and the Secondary Risk Screening Level (SRSL) for chloroform is $4 \mu\text{g}/\text{m}^3$.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

Michigan Department of Natural Resources, 1991. Response to the October 1990 Document on Chloroform Toxicity Submitted by Champion International Corporation.

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRSL, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

Jorgenson, T.A., E.F. Meierhenry, C.J. Rushbrook, R.J. Bull, and M. Robinson, 1985. Carcinogenicity of chloroform in drinking water to male Osborne-Mendel rats and female B6C3F₁ mice. *Fund. Appl. Toxicol.* 5:760-769.

NCI, 1976. Report on carcinogenesis bioassay of chloroform. Report No. (NIH) 76-1279. PB76-264018. National Cancer Institute. Bethesda, Maryland.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the IRSL and the SRSL.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The IRSL and SRSL for chloroform were developed by the Air Quality Division (AQD) of the Michigan Department of Environmental Quality (MDEQ).

The IRSL is based on an upper bound lifetime cancer risk of 10^{-6} , i.e., an excess lifetime cancer risk of 1 in 1,000,000, and the SRSL is based on an upper bound lifetime cancer risk of 10^{-5} , i.e., an excess lifetime cancer risk of 1 in 100,000. Unit risk is defined as the additional lifetime cancer risk occurring in a population in which all individuals are exposed continuously for life to a concentration of $1 \mu\text{g}/\text{m}^3$ of the chemical in the air they breathe.

In establishing IRSLs and SRSLs, priority is first given to using US EPA established inhalation cancer potency values. If the US EPA has established an inhalation cancer potency value for a chemical that is published in IRIS, that value is used to establish the IRSL and SRSL. In the case of chloroform, however, although the US EPA has established an inhalation cancer potency value, the unit risk value was determined by the AQD.

Following the submission of a document on chloroform toxicity by Champion International Corporation, the Michigan Department of Natural Resources (MDNR) reviewed the basis of the US EPA's cancer potency values. The US EPA Office of Drinking Water (ODW) had used the Jorgenson *et al.* (1985) drinking water study upon which to base the oral cancer potency for chloroform, while the US EPA's Office of Research and Development (ORD) has used the National Cancer Institute (NCI, 1976) study upon which to base the inhalation cancer risk value. The MDNR reviewed both studies and concluded that since rat kidney tumours were observed in both studies, and mechanistic data was not available to evaluate the influence on tumour incidence due to the different routes of exposure, an average of the slope factors from the Jorgenson *et al.* (1985) study rat kidney tumours and the NCI (1976) study male rat kidney tumours be used in the calculation of a cancer potency factor.

The recommended potency value is the geometric mean of the potencies derived from the Jorgenson *et al.* (1985) study and the NCI (1976) study. The MDEQ further concluded that the risk assessment performed by California obtained the more appropriate potency for the NCI study (2.6×10^{-2} (mg/kg/day)⁻¹). The US EPA IRIS potency value for the Jorgenson study that was used in the averaging process was 6.1×10^{-3} (mg/kg/day)⁻¹. The resultant geometric average is 1.3×10^{-2} (mg/kg/day)⁻¹. Based on the assumptions that the inhalation absorption factor is 65%, the average adult inhalation rate is 20 m³/day, and the average adult weight is 70 kg, this geometric average becomes 2.4×10^{-6} (µg/m³)⁻¹, which results in a 1 in one million lifetime cancer risk value of 0.4 µg/m³.

9. Key Risk Management Considerations:

The review of the risk assessment for chloroform was initiated by Champion International Corporation. Roy F. Weston, Inc., on behalf of Champion, established a Scientific Review Panel to review the risk assessment and present their conclusions to the MDNR. Several modifications to the MDNR's previous risk assessment were proposed, including a recommendation to use the Jorgenson *et al.* (1985) study instead of the NCI (1976) study upon which to base the cancer potency. Following a review of the document submitted by Champion International Corp., the MDNR determined that a mean potency value from the two studies was appropriate (MDNR, 1991).

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey has not set an air quality standard for chloroform (NJDEP, 1997a). However, New Jersey has accepted an inhalation Unit Risk Factor (URF) for chloroform of 2.3×10^{-5} ($\mu\text{g}/\text{m}^3$)⁻¹. This URF has been adopted from the Integrated Risk Information System (IRIS) of the United States Environmental Protection Agency (US EPA). The US EPA classifies chloroform as a probable human carcinogen (class B2 carcinogen).

4. *Application:*

The BAQEv Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

URF's are used in risk assessments to estimate the public health risks from the inhalation of carcinogens using the following equation:

$$\text{Incremental risk} = C \times \text{URF}$$

where C = maximum annual average ambient air concentration of a pollutant in $\mu\text{g}/\text{m}^3$
URF = pollutant-specific inhalation unit risk factor in $(\mu\text{g}/\text{m}^3)^{-1}$

As stated above, the URF for chloroform was adopted from IRIS. The maximum annual average ambient air concentrations of pollutants (C) are facility-specific and derived from one of three approaches: an initial risk screening assessment, dispersion modelling or air monitoring programs (NJDEP, 1997b). In the case of chloroform, air monitoring programs have little information on its annual average concentrations (NJDEP, 1997b).

For a specific carcinogen, AQPP considers the risk negligible if the incremental cancer risk is less than or equal to one in one million (1×10^{-6}), unacceptable if the incremental risk is greater than or equal to one in ten thousand (1×10^{-4}), and the risk is evaluated on a case-by-case basis by the AQPP if it is between one in one million and one in ten thousand.

9. Key Risk Management Considerations:

Not applicable.

10. Multimedia Considerations of Guidelines:

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. URFs must be used to calculate inhalation risks for carcinogens, while cancer potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, reference concentrations (RfCs) must be used for inhalation exposure, and reference doses (RfDs) for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. Other Relevant Factors:

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Chloroform (CAS# 67-66-3)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC) for chloroform is $980 \mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) for chloroform² is $0.04 \mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

NYSDEC, 1992. Memorandum to Matt Reis, Bureau of Application Review and Permitting, dated March 25, 1992. Subject: Toxicity Classification of Chloroform. Author: Carlos Montes, Bureau of Air Research. New York State Department of Environmental Conservation. Albany, New York.

Key Reference(s):

NIOSH. 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational

² In the process of reviewing the New York State Air Guidelines, the Department of Environmental Conservation indicated that the air guidelines were derived from a reference concentration (RfC) reported in the US EPA's IRIS database (NYSDEC, 1997a). However, a review of IRIS revealed that no RfC was available for chloroform. The agency was contacted for further clarification on the derivation of the SGC and AGC. At that time, the agency reported that the current AGC was adopted from the carcinogenic risk assessment conducted in IRIS. The summary here reflects the correct value for the AGC. The SGC is still current (NYSDEC, 1997b).

Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

US EPA, 1995. Integrated Risk Information System (IRIS) Computerised Database. . United States Environmental Protection Agency, Washington DC.

6. Peer-Review Process and Public Consultation:

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. Status of Guideline(s):

Current.

8. Key Risk Assessment Considerations:

Chloroform is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC was derived from NIOSH Short-Term Exposure Limit (STEL) (1988) by dividing the STEL by 10 (NYSDEC, 1991). NIOSH STEL was reported as 2 ppm (approximately equivalent to 9.80 mg/m³ at 25 °C and 1 atmosphere, molecular weight assumed as 119.4 g/mol). Under the 1991 New York State Air Guide - 1, the NIOSH STEL was considered a ceiling limit. Therefore, the SGC for chloroform was derived differently (using a factor of 10) than most other substances (usually an occupational limit is adjusted by 4.2 to account for continuous exposure).

$$\text{SGC} = 9.80 \text{ mg/m}^3 / 10 = 0.980 \text{ mg/m}^3 = 980 \text{ } \mu\text{g/m}^3$$

The AGC of 0.04 µg/m³ was adopted and derived from the US EPA carcinogenic unit risk estimate of $2.3 \times 10^{-5} (\mu\text{g/m}^3)^{-1}$ for chloroform (assumes an extra life-time risk of one in 1,000,000).

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guideline considers only human exposure to contaminants in air.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

None.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*

Not applicable.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)
2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Chloroform is classified as a class 1 gaseous organic substance (g.O1). This classification imposes an emission standard of 20,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 0.10 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992). The environmental quality objectives program sets a negligible effects target concentration of 1 $\mu\text{g}/\text{m}^3$ for average annual air emissions for chloroform. The Netherlands has also adopted a maximum immissible (sic) concentration (MIC) of 7.5 $\mu\text{g}/\text{m}^3$ from the regional MIC developed by the province of Groningen.

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long-term environmental quality objective which establishes a target value below which emissions of priority substances must be maintained. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological

literature. This progressive approach will require facility-specific emissions to be kept below a limit or guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance or limit values are either air quality statutory requirements or non statutory regional-specific MIC levels.

5. Documentation Available:

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. Peer-Review Process and Public Consultation:

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 20,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 0.10 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

The regional MIC values applied in the environmental quality objectives program were derived by the Province of Groningen using the occupational hygiene-based national 1982-1983 Maximum Acceptable Concentration's (MACs) adjusted by a modifying factor. A modifying factor of 1000 is applied for compounds classified by the International Agency for Research on Cancer (IARC) as a substance which may have carcinogenic properties, or for compounds which have been shown to cause reproductive or developmental effects. A factor of 150 was applied for all other substances. The MAC's from which the MIC's are derived are occupationally-based exposure limits and these uncertainty factors account for the extrapolation from a 40-hour work week to a continuous 24-hour exposure level, and to adjust for exposure to the general population (children, adults and the elderly).

The negligible effects target value of $1 \mu\text{g}/\text{m}^3$ (annual average) was derived from the recommended toxicological limit value reported in the Integrated Criteria Document for Chloroform published by the National Institute for Public Health and Environmental Protection (RIVM) and from advice by the National Health Council (Directorate-General for Environmental Protection, 1997).

9. *Key Risk Management Considerations:*

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Chloroform (CAS# 67-66-3)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. Chemosphere 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} . No assessment has been carried out for chloroform.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Chloroform (CAS # 67-66-3)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. Chloroform has not been assessed or evaluated under the first Priority Substance List (PSL1). It was nominated as a substance for consideration, and has been recommended for evaluation by the Ministers' Expert Advisory Panel under the Second Priority Substance List (PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Chloroform is present in drinking water as a by-product of water treatment by chlorination, and is found in food and in the atmosphere. It is also used in a variety of industrial applications. It has been shown to be both carcinogenic and genotoxic in animals, and studies have demonstrated potential

evidence that it is carcinogenic in humans. Based on a needs assessment completed by the Ministers' Expert Advisory Panel, chloroform was one of twenty five substances which was selected for evaluation under PSL2. This evaluation will entail a detailed review of the literature in order to characterize the level of exposure, and the associated risks to human health and the environment in Canada from exposure to chloroform.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
ETHYL BENZENE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which air standards will be reviewed over the next several years. Ethyl benzene was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that has been published subsequent to the development of the existing standard in 1975. A review of the scientific and technical information relevant to setting an ambient air quality standard for ethyl benzene has previously been provided to stakeholders for their comments. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour point of impingement (POI) standard for ethyl benzene.

Ethyl benzene, CAS #100-41-4 is a clear and colourless flammable liquid with a sweet smelling, gasoline-like aromatic odour. It is reported to have an odour threshold of 1900 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre). Ethyl benzene is primarily used as an intermediate in styrene, rubber, latex, and plastics manufacturing. It is also used as a solvent and as raw material in the synthetic chemical, petroleum industries and as a diluent in pesticide and paint manufacturing. Ethyl benzene is a naturally occurring product of biomass combustion, and a component of crude oil. It enters the atmosphere primarily through fugitive industrial emissions and auto exhaust fumes as a result of its use in gasoline products. Ethyl benzene also enters the environment as a result of the use of technical grade xylene which can contain up to 20% ethyl benzene. Ethyl benzene may also be accidentally released into the environment through spills in areas where it is produced and/or near industries that use this compound.

Data from the National Pollutant Release Inventory (NPRI) of Environment Canada indicated that most ethyl benzene emissions were to air (e.g. >98% of total releases). There have been slight increases in atmospheric releases of ethyl benzene in Canada through the 1993 to 1997 reporting years. In comparison to the national emissions of ethyl benzene, increases in Ontario have been more noticeable during the 1993 to 1997 reporting years. Ontario contributed to approximately 65% of the national atmospheric releases. In 1997 the national release to air was reported to be 817.2 tonnes, the release in Ontario was 531 tonnes.

Absorption of ethyl benzene occurs mainly through the lungs and secondarily through the skin. Once absorbed, ethyl benzene is metabolized mainly to mandelic, hippuric and phenylglyoxylic acids, all of which are eliminated in urine 6-10 hours following absorption.

Chronic exposure to elevated levels of ethyl benzene is irritating to the eyes, nose and throat, and can cause nausea, headaches, vomiting and central nervous system effects. There is limited information on

the developmental or reproductive toxicity of ethyl benzene in humans. Although, it has been shown that ethyl benzene is toxic to the fetuses of rats and rabbits.

The International Agency for Research on Cancer has not classified ethyl benzene as a carcinogen and the United States Environmental Protection Agency (US EPA) has concluded there was insufficient data to determine the carcinogenic potential of ethyl benzene. However, a recent 2-year study on rats and mice completed by the National Toxicological Program suggests that there is clear evidence of ethyl benzene's carcinogenicity in these test animals.

Ontario currently has air quality standards for ethyl benzene. The half-hour POI standard and the 24-hour AAQC are both set at $4,000 \mu\text{g}/\text{m}^3$. These criteria were established based on odour concerns. Documentation from ten agencies including: the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government were reviewed for the existence and basis of air quality criteria for ethyl benzene.

These ten agencies based their current guidelines on the avoidance of adverse developmental effects. The US EPA has established a reference concentration (RfC) of $1000 \mu\text{g}/\text{m}^3$. The reference concentration is an estimate of daily exposure which is likely to be without appreciable risk over a lifetime. Massachusetts, Michigan, New Jersey and New York have developed reference concentrations or ambient air quality guidelines for ethyl benzene based on the RfC from the US EPA. California is proposing to adopt the RfC from the US EPA for its chronic criterion.

Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the RfC by the United States Environmental Protection Agency. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for ethyl benzene based on the rationale for the RfC of the US EPA and also the odour property of this compound.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for ethyl benzene:

- **a 24-hour average AAQC of $1,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the adverse health effects of this compound;**
- **a 10 -minute average AAQC of $1,900 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the odour nuisance of this compound; and,**

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- **a half-hour average POI standard of 1,400 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the odour nuisance of this compound.**

Since ethyl benzene is a commonly used substance in various industries in Ontario, immediate compliance with this proposed POI standard may be difficult for some industries. Stakeholder comments are requested regarding any technical and/or economic impacts that may be encountered as a result of the revised POI standard. The comments received from stakeholders will help to determine whether or not risk management is required and if so, its extent.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Ethyl benzene was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing standard in 1975. A review of scientific and technical information relevant to setting an ambient air quality standard for ethyl benzene had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for ethyl benzene.

2.0 General Information

2.1 Physical/chemical Properties

The following list provides some general information on ethyl benzene and its properties:

CAS #	100-41-4
RTECS #	DA0700000
UN #	1175
Conversion Factor	1 ppm = 4.34 mg/m ³ @ 25 °C and 1 atm 1 mg/m ³ = 0.23 ppm @ 25 °C and 1 atm
Boiling Point	136.2 °C @ 760 mmHg
Flash Point	21 °C
Henry's Law Constant	8.7x10 ⁻³ @ 3 atm/mole
Log K _{ow}	3.15
Formula	C ₈ H ₁₀
Molecular Weight	106.16
Vapour Density (air = 1)	3.66
Vapour Pressure	9.53 mmHg @ 25 °C
Common Synonyms	Ethyl benzene, Ethylbenzol, Phenylethane, Phenylethylene, EB

Ethyl benzene is a clear and colourless flammable liquid, with a sweet, gasoline-like aromatic odour (HSDB, 1997). An odour threshold (50% detection) of 1.9 mg/m³ (1900 µg/m³) has been reported (Nagy, 1991). The reported odour thresholds range from 398 µg/m³ to 2600 µg/m³ (AIHA, 1989).

2.2 Uses of Ethyl Benzene

Ethyl benzene has several industrial applications. It is primarily used as an intermediate in styrene, rubber, latex and plastics manufacturing (CCINFO, 1992). It is also used as a solvent and raw material in synthetic chemical, petroleum, and gasoline industries (CESARS, 1991), and is used as a diluent in pesticide and paint manufacturing (HSDB, 1997).

2.3 Sources and Levels

Sources

Ethyl benzene is a naturally occurring product of biomass combustion, and a component of crude oil (HSDB, 1997). It enters the atmosphere primarily through fugitive emissions and exhaust as a result of its use in gasoline products (HSDB, 1997). Ethyl benzene also enters the environment as a result of its use in technical grade xylene, which can contain up to 20% ethyl benzene (Calabrese and Kenyon, 1991). Ethyl benzene may be accidentally released into the environment through spills, connected with its production and industrial use (HSDB, 1997). Ethyl benzene is listed in the National Pollutant Release Inventory (NPRI) of Environment Canada for the emissions of chemicals based on information provided by reporting facilities (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996, NPRI, 1997). Releases of ethyl benzene have been increasing in Canada (e.g. 615 tonnes in 1993 to 817 tonnes in 1997). The increases in the releases in Ontario have been more apparent (338 tonnes in 1993 to 531.6 tonnes in 1997). Of the ten facilities in Canada releasing the highest amounts of ethyl benzene, seven were in Ontario (NPRI, 1994). In 1995, 1996 and 1997, eight of the ten highest emitting facilities were in Ontario. Ontario's contribution to the total Canadian releases was 66% (1994), 75% (1995), 72% (1996) and 65% (1997). In 1997, 30 Ontario industrial sources released 531.6 tonnes of ethyl benzene to the atmosphere. In the past five reporting years (1993 - 1997), of the total environmental releases, more than 98% of ethyl benzene was released to the atmosphere. The majority of these releases originated from the manufacturers of rubber products, motor vehicles, motor vehicle parts, refined petroleum and plastic products, and chemicals.

Ambient Air Concentrations

Environment Canada has collected ambient air data for ethyl benzene from January 1993 to December 1995 from 39 monitoring stations across Canada (Environment Canada, 1997). From 4,230 samples, a mean concentration of $1.19 \pm 1.40 \mu\text{g}/\text{m}^3$ was observed (Environment Canada, 1997). The concentrations reported ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $46.50 \mu\text{g}/\text{m}^3$ (Environment Canada, 1997). Results of joint monitoring activities in Ontario by Environment Canada and the MOE indicated that for the period of 1990-95, the single largest 24-hour average concentration was found to be approximately $142 \mu\text{g}/\text{m}^3$; the second largest concentration was approximately $52 \mu\text{g}/\text{m}^3$. Unscheduled monitoring of ethyl benzene, by the MOE, indicated that half-hour average concentrations in Ontario ranged from 0.01 to $220 \mu\text{g}/\text{m}^3$ (MOEE, 1997). Maximum levels were detected at chemical waste facilities in Elmira and Sarnia, at concentrations of $220 \mu\text{g}/\text{m}^3$ and $49 \mu\text{g}/\text{m}^3$, respectively (MOEE, 1997).

From an analysis of recent applications for Certificate of Approval in Ontario, a sample of 60 facilities that emit ethyl benzene were identified. These approvals were for emissions from facilities in the

automotive spray paint and parts, adhesives and plastic products industries. The median Ground Level Concentration, estimated by Regulation 346 dispersion modelling, for all 60 sources was $10.5 \mu\text{g}/\text{m}^3$. The maximum and minimum were 335 and $0.002 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

In the atmosphere, ethyl benzene exists primarily in the vapour phase and has a photochemical half-life of 0.5 to 2 days (HSDB, 1997). It is not subject to direct photolysis (HSDB, 1997). Releases of ethyl benzene in either soil or water will evaporate into the atmosphere. This is a result of its moderate propensity for adsorption to soil, it is also likely that its biodegradation will be slow following acclimation of ambient microorganisms (HSDB, 1997). Ethyl benzene released in water will decrease through evaporation and biodegradation. A half-life in water of 2 days to 2 weeks is possible, depending on the season and the primary loss processes (HSDB, 1997). A small amount of ethyl benzene may be adsorbed in the sediment, but significant bioconcentration in aquatic organisms is not expected based on its octanol-water partition coefficient. It will not hydrolyze in either soil or groundwater (HSDB, 1997).

3.0 Toxicology of Ethyl Benzene

The following toxicological review of ethyl benzene is primarily focussed on the inhalation route of exposure, as this is the predominant exposure pathway for humans, and since more than 98% of the emitted ethyl benzene is released to air (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996). Data on other exposure media are included where relevant, or where inhalation data are lacking.

Absorption of ethyl benzene occurs primarily through the lungs and secondarily through the skin (HSDB, 1997). In both human and animal studies, approximately 40 - 60% of the inhaled ethyl benzene was retained in the body (reviewed by ATSDR, 1997). It has been demonstrated that about 2% of the total amount of inhaled ethyl benzene is absorbed in the adipose tissue of humans and animals (ATSDR, 1997). In rats, distribution of inhaled ethyl benzene is rapid and efficient. Forty eight hours after the animals were exposed to 230 ppm ($998 \text{ mg}/\text{m}^3$) of the radioactive derivative of this compound, the highest concentrations were found in the carcass, liver, and gastrointestinal tract and with lower amount recovered in the adipose tissue (ATSDR, 1997). When administered subcutaneously to rats (2.5 mL, 1:1 v/v), ethyl benzene was absorbed and detected in the blood within 2 hours. Levels of 10 - 15 ppm (or mg/L) ethyl benzene was maintained in the blood for 16 hours (HSDB, 1997). Once absorbed, ethyl benzene is metabolized mainly to mandelic, hippuric and phenylglyoxylic acids. However, the metabolism of ethyl benzene differs in humans and rodents (Engstrom *et al.*, 1984 as cited in US EPA, 1998). The major metabolites in humans are mandelic acid and phenylglyoxylic acid, whereas these are minor metabolites in rats and rabbits (Kiese and Lenk,

1974 as cited in US EPA, 1998). Elimination in urine was highest 6-10 hours following absorption (HSDB, 1997; CESARS, 1991).

The general systemic effects observed in humans are pulmonary and ocular irritation and possible haematological changes; in animals, the target organs appear to be the lungs, liver and the kidney, with transient effects on the haematological system; neurological and developmental effects have also been reported (see no-observed-adverse-effect levels, NOAEL, reviewed in ATSDR, 1997).

3.1 Acute Toxicity

Ethyl benzene vapours are slightly irritating to the nose and throat (HSDB, 1997), and inhalation of higher concentrations may cause nausea, headaches, vomiting and central nervous system (CNS) depression in humans. Exposure to 435 mg/m³ of ethyl benzene has been reported to result in drowsiness, ataxia, and mild to severe vertigo (CCINFO, 1992). At acute exposure levels exceeding 4,350 mg/m³, ethyl benzene has been reported to cause severe ocular irritation leading to tearing and reddening of the eyes (Calabrese and Kenyon, 1991). Exposure to vapour levels exceeding 21,750 mg/m³ causes intolerable irritation of the eyes, nose and throat (HSDB, 1997).

The inhalation LC₅₀ (lethal concentration, 50% killed) for rats has been reported to be 4,000 ppm (17360 mg/m³) or 13367 ppm (58013 mg/m³) (reviewed by ATSDR, 1997). Ethyl benzene-induced lethality varies among different animal species. When Fischer 344 rats, B6C3F₁ mice and New Zealand White rabbits were exposed to 0, 400, 1200, 2400 ppm (0, 1740, 5220, 10440 mg/m³) of ethyl benzene for 6 hours a day, for 4 days, mortality occurred in mice at half the dose (5220 mg/m³) required to cause death in rats (10440 mg/m³); all rabbits in each exposure group survived (Biodynamics, 1986 and Vragg *et al.*, 1989 as cited in ATSDR, 1997).

3.2 Subchronic/Chronic Toxicity

Chronic exposure to elevated levels of ethyl benzene is irritating to the eyes, nose and throat (CCINFO, 1992). Chronic inhalation of ethyl benzene mimics its acute effects, causing nausea, headaches, vomiting and CNS toxicity (CCINFO, 1992). Ethyl benzene may also cause mild renal, blood and testicular toxicity, as well as chronic inflammation of the upper respiratory tract (HSDB, 1997). Prolonged or repeated skin contact with ethyl benzene may cause dermatitis, reddening of the skin, and hair loss (CCINFO, 1992). Individuals with existing skin disorders, liver, kidney, nervous system, blood and haemopoietic-organ disorders, and women with ovulation and menstrual cycle disorders, may be more susceptible to the chronic adverse effects of ethyl benzene (ARB, 1996).

Detailed information on animals has been summarized in ATSDR (1997) and by the WHO (1996). In general, no mortality was observed in Rhesus monkeys exposed to ethyl benzene at 400 ppm (1740

mg/m³) or 600 ppm (2610 mg/m³) for 7 to 8 hours per day, 5 days a week for 6 months. Similarly, no deaths were observed in rats exposed for the same schedule at 0, 400, 600, 1250 or 2200 ppm (0, 1740, 2610, 5425 or 9550 mg/m³); guinea pigs and rabbits were exposed up to 1250 ppm (5425 mg/m³) for 7 - 8 hours/day, 5 days/week for 6 - 7 months, in neither case were deaths observed. (Wolf *et al.*, 1956 as cited in ATSDR, 1997). Increased mortality in some rats was noted only at the highest exposure concentration (750 ppm or 3250 mg/m³) in a 2-year study (NTP, 1992 as cited in ATSDR, 1997). The target organs for the general systemic effects of ethyl benzene appear to be the lung, liver and kidney ATSDR, 1997).

3.3 Developmental/Reproductive Toxicity

There is limited information on the developmental or reproductive toxicity of ethyl benzene in humans. Testicular degeneration has been suggested as a potential adverse effect of exposure to ethyl benzene (Calabrese and Kenyon, 1991).

The developmental and reproductive toxicity of ethyl benzene was investigated in both Wistar rats (78 - 107 animals/concentration) and New Zealand white rabbits (29 - 30 animals/concentration). Both animal species were exposed to ethyl benzene concentrations of 0, 435 and 4350 mg/m³ (0, 100 and 1000 ppm) through inhalation, 6-7 hours/day during days 1 to 19 and 1 to 24 of gestation, respectively (Calabrese and Kenyon, 1991; Andrew *et al.*, 1981 as cited in US EPA, 1998). In addition, a separate group of rats was exposed for 3 weeks prior to mating, and exposure was continued into the gestational period. Pregnant rats were sacrificed on day 21 and pregnant rabbits were sacrificed on day 30. Maternal organs, such as the liver, lungs, kidney, heart, spleen, adrenals, ovaries and brain were examined for histologic changes. Uteri and fetuses were examined for possible abnormalities.

Ethyl benzene did not elicit embryotoxicity, fetotoxicity or teratogenicity in rabbits at any exposure level. No major malfunctions or minor abnormalities or common variants were found in fetal rabbits. A statistically significant reduction in the number of live kits per litter (7 ± 3 , s.d. vs control, 8 ± 3 , s.d.) was found at both exposure levels. However, there was no statistically significant increase in the number of dead or resorbed fetuses when compared to the controls. Examination of pre-natal mortality ranged from 5 - 8%, and pre-implantation loss ranged from 18 - 27% did not result in a concentration-related intrauterine mortality. There was no clear evidence of reduced fertility in the rabbits exposed to ethyl benzene.

Rats exposed to ethyl benzene during pregnancy did not show signs of histopathological changes in maternal organs. No effect on fertility or any reproductive abnormalities were noticed. Both the absolute and relative liver, kidney and spleen weights of the pregnant rats were significantly increased in the high exposure group. There was a significant increase in the incidence of supernumerary and rudimentary ribs in the fetuses of rats exposed to the high concentration, and an elevated incidence of

extra ribs in the fetuses of both the high and low exposure groups (Andrew *et al.*, 1981 as cited in US EPA, 1998).

In the pre-gestational exposure group, 3 weeks prior to mating and throughout the gestational period, a significantly increased incidence of extra ribs was observed only in the high exposure level (1000 ppm or 4350 mg/m³) group. There was no incidence of rudimentary ribs in any of the exposed groups. When extra and rudimentary ribs were grouped for analysis, there was no significant increase in supernumerary ribs in any of the exposed groups. The lack of observed increase in supernumerary ribs may be due to the fewer number of litters examined in the pre-gestationally exposed group. No fetal toxicity was noted in either exposure groups. No signs of histopathological changes were observed in maternal organs. No effect on fertility or any reproductive abnormalities were noticed. The absolute and relative liver and spleen weights were significantly increased in pregnant rats exposed to 1000 ppm (4350 mg/m³), only the relative kidney weight was increased significantly.

3.4 Genotoxicity

Ethyl benzene (0.4 mg/plate) and its common metabolites¹ were not mutagenic to *Salmonella typhimurium* strains TA98, TA1535, TA1537, and TA1538, with or without metabolic activation (Calabrese and Kenyon, 1991; Nestmann *et al.*, 1980 as cited in US EPA, 1998). In a battery of short-term mutagenic tests including bacterial mutation assays, mitotic gene conversion in *Saccharomyces cerevisiae* JD1 in the presence and absence of metabolic activation, and those quantifying the frequency of recessive lethal mutations in *Drosophila melanogaster*, chromosomal damage in rat liver epithelial cells, and oncogenic transformation in Syrian hamster embryo cells, all gave negative findings (reviewed in CESARS, 1991 and US EPA, 1998). Ethyl benzene induced a significant increase in the number of sister chromatid exchanges in human lymphocyte cultures at a concentration of 10 mmol/L without metabolic activation (US EPA, 1998).

There was only one study available on the genotoxic effects of inhaled ethyl benzene in humans. A low-level ethyl benzene exposure was studied in the peripheral lymphocytes of workers in a styrene production plant (Holz *et al.*, 1995 as cited in ATSDR, 1997). Twenty five exposed and 25 non-exposed workers were selected for the study. Active air sampling at four sites (oven house, production control, storage facility and distillation area) showed that the ethyl benzene concentrations for exposed workers ranged from 365 to 2340 mg/m³ (84 - 539 ppm). At the pump house, the ethyl benzene concentrations were greater than 4000 mg/m³ (921 ppm). Control workers were exposed to 145 - 290 mg/m³ (33 - 67 ppm) ethyl benzene. Genotoxic studies included DNA adducts in peripheral blood monocytes, DNA single strand breaks, sister chromatid exchange and micronuclei in lymphocytes.

¹The common metabolites were not listed in the source document. However, mandelic acid, hippuric acid, and phenylglyoxylic acid are known common metabolites of ethyl benzene.

Absorption of ethyl benzene was confirmed by urinary metabolite measurements. No genotoxic effects related to exposure were observed by DNA adduct formation, or DNA single strand break and sister chromatid exchange. However, there were increased kinetochore positive micronuclei in peripheral lymphocytes in the total exposed group, exposed smokers and exposed non-smokers, the frequency of total micronuclei in peripheral lymphocytes was unchanged.

3.5 Carcinogenicity

The US EPA has classified ethyl benzene in the Group D (not classifiable) category for the reason of insufficient evidence from animal bioassay and epidemiological data to support a carcinogenic potential for this compound (US EPA, 1998). The International Agency for Research on Cancer (IARC) has not classified ethyl benzene as a carcinogen (ARB, 1996).

There was only one study available which monitored the cancer development in 200 male workers chronically exposed to ethyl benzene (Bardodej and Cirek, 1988 as cited in ATSDR, 1997). In a period of 20 years, no cases of malignancy in the workers were reported. No conclusions can be drawn from this study because no quantitative information for exposure was provided and the duration chosen for tumour observation was short, and therefore was insufficient for detecting long-latency tumours in humans. No other studies were available regarding cancer incidence and ethyl benzene exposure in humans (ATSDR, 1997).

The National Toxicology Program (NTP) has recently completed a 2-year ethyl benzene inhalation study in rats and mice (NTP, 1996). Fischer 344/N rats and B6C3F₁ mice of both sexes were exposed to 0, 75, 250 or 750 ppm (0, 326, 1088 or 3263 mg/m³) ethyl benzene for up to 2 years. Incidences of renal tubular adenoma and adenoma or carcinoma (combined) were significantly higher in male Fischer 344/N rats exposed to ethyl benzene at 3263 mg/m³ than those in the control group. An extended examination showed significant increases in the occurrence of renal tubule adenoma and renal tubule hyperplasia, in both male and female Fischer 344/N rats exposed to 3263 mg/m³. The severity of neuropathy was also increased in both male and female rats exposed to this concentration. The incidences of interstitial cell adenoma and bilateral testicular adenoma in males exposed to 3263 mg/m³ were significantly higher than that of the control group, but were slightly higher than the NTP historical control range. The tumours (adenoma) observed were: 36/50, 33/50, 40/50 and 44/50 in male rats exposed to 0, 326, 1088 and 3263 mg/m³ respectively.

In the mice, incidences of alveolar/bronchiolar adenoma and alveolar/bronchiolar adenoma or carcinoma (combined) were significantly higher in males exposed to 3263 mg/m³ than in the controls, but were within the NTP historical control range. The incidences of hepatocellular adenoma and hepatocellular adenoma or carcinoma (combined) were significantly greater in female mice exposed to 3263 mg/m³ than in control mice, but were within the historical control range. Results of these NTP

studies indicate that there is evidence of carcinogenicity in male rats, and some evidence of carcinogenicity in female rats and in male and female mice (NTP, 1996). The draft technical report was reviewed at a meeting of the NTP Board of Scientific Counsellor's Technical Reports Review Subcommittee held on December 11, 1996. Details of the study are summarized under Other Relevant Factors in Section 11.1, Federal Government of the United States.

3.6 Environmental Effects

Exposure of earthworms to ethyl benzene in artificial soil resulted in a no-observed-effect-concentration (NOEC) of 73 mg/kg and a lowest-observed-effect-level (LOEC) of 192 mg/kg (Environment Canada, 1994). A contact (the effects of ethyl benzene applied directly to a filter paper to which earthworms were exposed) experiment reported a 48-hour LC_{50} of 4.93 μ g/kg for earthworms (*Esenia foetida*) exposed to ethyl benzene (Callahan *et al*, 1994).

Ethyl benzene exposure is detrimental to vegetable growth. Studies of seedling emergence in radishes exposed to ethyl benzene for 72 hours, found the NOEC to be 4.7 mg/kg, while the LOEC concentration was 9.3 mg/kg. Effects upon seedling emergence in lettuce plants, resulting from a 120-hour ethyl benzene exposure were observed; a LOEC at 4.7 mg/kg and an effective concentration (EC_{50} ; 50% of the population is affected) at 7.6 mg/kg (Environment Canada, 1996).

Ethyl benzene appears to be of low to moderate acute toxicity to aquatic organisms (WHO, 1996). Ninety six-hour LC_{50} values for aquatic organisms range from 2.6 mg/L for mysid shrimp (*Mysidopsis bahia*) (Masten *et al*, 1984) to 9.2 mg/L for guppy, (*Poecilia reticulata*) (Galassi *et al*, 1988). Information regarding the chronic exposure of ethyl benzene to aquatic organisms is not available.

The phytotoxic potential of ethyl benzene was evaluated in green and blue algae using a cell multiplication inhibition test. The threshold for toxicity for green algae was determined to be 160 mg/L and 33 mg/L for blue algae (CESARS, 1991). A study of the inhibition of cell multiplication in bacteria, *Pseudomonas putida*, determined a toxicity threshold of 12 mg/L for ethyl benzene exposures (Bringmann *et al*, 1980).

4.0 Existing Air Quality Criteria

4.1 Overview

Ontario currently has air quality standards for ethyl benzene. The half-hour POI standard and the 24-hour AAQC are both $4,000 \mu\text{g}/\text{m}^3$ (approximately 1 ppm). These criteria were established based on the odour effects of ethyl benzene (MOEE, 1994a).

The documentation from ten agencies (the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government) was reviewed for the existence and basis of air quality criteria for ethyl benzene. A brief summary of this review is presented in Table 1 and agency-specific summaries of information concerning air quality guidelines for ethyl benzene are presented in the Appendix (section 11.0).

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE normally uses a factor of 15 to convert from criteria based on annual average concentrations to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of the ten agencies, the US EPA, the Commonwealth of Massachusetts, the States of Michigan, New Jersey, and New York, and The Netherlands have all developed criteria or reference values for ethyl benzene. The US EPA has developed an inhalation Reference Concentration (RfC) of $1,000 \mu\text{g}/\text{m}^3$ for ethyl benzene. This RfC is based on studies of developmental effects in rats and rabbits. The Commonwealth of Massachusetts derived their Threshold Effects Exposure Limit (TEL) and Allowable Ambient Limit (AAL) of $300 \mu\text{g}/\text{m}^3$ from the US EPA's "calculated"² RfC of $1,447 \mu\text{g}/\text{m}^3$. The States of Michigan and New York based their Initial Threshold Screening Level (ITSL; $1,000 \mu\text{g}/\text{m}^3$) and Annual Guideline Concentration (AGC; $1,000 \mu\text{g}/\text{m}^3$), respectively, on the US EPA's RfC. The State of New Jersey also adopted this RfC of $1,000 \mu\text{g}/\text{m}^3$ for use in permitting applications. The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency has recently proposed

²The US EPA's calculations led to a value of $1,447 \mu\text{g}/\text{m}^3$, which was rounded down to $1,000 \mu\text{g}/\text{m}^3$, the final RfC value published in the IRIS database. For further information on the derivation of the RfC, please refer to the Agency-Specific Summary in Section 7.1, Federal Government of the United States.

Table 1. Summary of Existing Air Quality Guidelines^[1] for Ethyl Benzene

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA (IRIS)	RfC (Reference Concentration): 1,000 µg/m ³ .	Studies of developmental effects in rats and rabbits.	1990	
California	Proposed chronic REL of 1000 µg/m ³	RfC from US EPA	1997	Development, alimentary system and kidney effects
Massachusetts	TEL (Threshold Effects Exposure Limits): 300 µg/m ³ (24-hour average).	"Calculated" RfC from US EPA. ^[3]	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 300 µg/m ³ (annual average).	"Calculated" RfC from US EPA. ^[3]	1995	
Michigan	ITSL (Initial Threshold Screening Level): 1,000 µg/m ³ (24-hour average).	RfC from US EPA.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC: 1,000 µg/m ³ (24-hour).	RfC from US EPA.	1994	Permitting application. The RfC must be used in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): 100,000 µg/m ³ (1-hour average).	TLV-TWA from ACGIH.	1997	Used for permitting.
	AGC (Annual Guideline Concentration): 1,000 µg/m ³ .	RfC from US EPA.	1997	Used for permitting.
WHO	None.			
Netherlands	100,000 µg/m ³ (half-hour average).	Emission standard.	1994	Used for permitting.
	National MIC (Maximum Immissions Concentration): 240 µg/m ³ (annual average).	Province of Groningen's guideline.		
Sweden	None.			
CEPA	None.			

Ontario	half-hour POI standard: 4,000 $\mu\text{g}/\text{m}^3$. 24-hour AAQC: 4,000 $\mu\text{g}/\text{m}^3$.	Both the POI and AAQC are based on odour.	1994	
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1. Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
2. Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.
3. Massachusetts applied adjustments to the "calculated" RfC of 1,447 $\mu\text{g}/\text{m}^3$ as opposed to the US EPA's final RfC of 1,000 $\mu\text{g}/\text{m}^3$.

to derive its chronic inhalation reference level of 1,000 $\mu\text{g}/\text{m}^3$, based on the RfC of the US EPA (OEHHA, 1997). New York has also established a Short-term Guideline Concentration (SGC) of 100,000 $\mu\text{g}/\text{m}^3$ based on the Threshold Limit Value-Time Weighted Average (TLV-TWA) of the American Conference of Governmental Industrial Hygienists (ACGIH). The Netherlands has set an emission standard of 100,000 $\mu\text{g}/\text{m}^3$ for ethyl benzene, which is used for permitting applications and a National Maximum Immissions Concentration (MIC) of 240 $\mu\text{g}/\text{m}^3$ based on the Province of Groningen's guideline.

The World Health Organization (WHO), Sweden, and the Canadian Federal Government have not established air quality criteria for ethyl benzene. A tentative guideline of 22 mg/m^3 has been proposed for ethyl benzene by the WHO (1996), based on effects on liver weight increases in animals.

None of these agencies have considered the carcinogenic potential of ethyl benzene in their criteria development.

4.2 Evaluation of Existing Criteria

It appears that most of the agencies support the risk assessment performed by the US EPA on the developmental effects of ethyl benzene through the inhalation route of exposure. These agencies have adopted (Michigan, New Jersey, New York), proposed to adopt (California) or have derived from (Massachusetts) the RfC of 1 mg/m^3 (1,000 $\mu\text{g}/\text{m}^3$) developed by the US EPA as their ambient air quality criteria.

The US EPA has established an inhalation RfC for ethyl benzene based on the developmental effect of this compound. Two critical studies were used to derive this criterion (Andrew *et al.*, 1981 and Hardin *et al.*, 1981). In the Andrew *et al.* (1981) study, Wistar rats and New Zealand white rabbits were exposed to nominal concentrations of 0, 100 or 1,000 ppm (0, 435 or 4,350 mg/m^3) ethyl benzene for

6-7 hours/day, 7 days/week during gestation days 1-19 (for rats) and 1-24 (for rabbits) (see section 3.3 for details). Maternal toxicity was not evident at either exposure levels. The principal observed effect in rabbits was a reduced number of live rabbit kits per litter at both ethyl benzene concentrations. Re-analysis of the data from Andrew *et al.*, (1981), the US EPA indicated that there was no difference in the numbers of live rabbit kits per litter between animals exposed to 435 mg/m³ and the control rabbits (US EPA, 1998). Thus, the 435 mg/m³ was considered a NOAEL, and the 4,350 mg/m³ a LOAEL. The data from rats also suggested a LOAEL of 4350 mg/m³ for the increased incidence of supernumerary and rudimentary ribs in the fetuses, as well as increases in the absolute and relative weights in liver, kidney and spleen in the dams exposed to 4350 mg/m³. A NOAEL of 435 mg/m³ for the lack of increased incidence of supernumerary and rudimentary ribs in the fetuses was recommended. The data from rats exposed to the same concentrations of ethyl benzene, for 3 weeks before mating and also during gestation period appeared to support the findings. Rats exposed only during gestation resulted in significant increases in absolute and relative kidney, liver and spleen weights. However, significant increases in relative organ weight were observed only in the kidneys of pre-gestationally exposed rats.

Based on these observations, the US EPA has suggested a NOAEL of 435 mg/m³ for the lack of developmental effects of ethyl benzene in rats and rabbits. The US EPA did not consider an adjustment for exposure period for developmental effects. As a result of the lack of information in extrapolating exposure dosimetry from animals to humans, based on gas:respiratory effects, the calculated human equivalent NOAEL was determined to be unchanged, 435 mg/m³. The LOAEL was determined to be 4350 mg/m³.

In deriving the RfC for ethyl benzene, the US EPA (1998) applied an uncertainty factor (UF) of 300 to the NOAEL (435 mg/m³). A factor of 10 to account for the protection of sensitive individuals a factor of 10 to adjust for the absence of multigenerational reproductive and chronic studies and a factor of 3 to extrapolate between species (UF=3). The RfC for ethyl benzene was calculated as 1.447 mg/m³, and rounded down to 1 mg/m³:

$$\text{RfC} = 435 \text{ mg/m}^3 / 300 = 1.447 \text{ mg/m}^3 \text{ or } 1 \text{ mg/m}^3$$

Confidence in the principal study, the overall database of toxicological information and the inhalation RfC for ethyl benzene is reported as low. Although the developmental study by Andrew *et al.* (1981) was considered a well conducted and it indicated no adverse effects in either species tested (at the NOAEL level), the study was given a low confidence rating. More information on potential maternal toxicity and other developmental effects may have been elicited by higher exposure concentrations. The database was given a low confidence rating due to a lack of chronic and multigenerational studies. Since the confidence in both the principal study and the database was low, the confidence in the RfC is also considered low.

The States of Michigan, New Jersey, New York (for their AGC) and the Commonwealth of Massachusetts (MDEP) agreed with the risk assessment of the US EPA, as a result they have promulgated air quality guidelines for ethyl benzene based on the US EPA's RfC. Michigan, New Jersey and New York adopted the RfC value of $1,000 \mu\text{g}/\text{m}^3$ directly as their respective criteria. The California Environmental Protection Agency agreed with the assessment of the US EPA on the developmental effects of ethyl benzene and proposed to adopt the RfC as its chronic inhalation reference exposure level ($1,000 \mu\text{g}/\text{m}^3$; annual averaging time).

The MDEP of Massachusetts derived its TEL from the RfC value of $1,447 \mu\text{g}/\text{m}^3$ without rounding. This value was divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure. The TEL was, therefore, calculated as $289.4 \mu\text{g}/\text{m}^3$ and was then rounded up to $300 \mu\text{g}/\text{m}^3$.

The MDEP reported that there was insufficient evidence to classify ethyl benzene as a carcinogen based on its carcinogenic and mutagenic potentials (MDEP, 1990). However, the MDEP has summarized ethyl benzene's positive score for structure-activity relationships (SAR) analysis. The non-threshold effect exposure limit (NTEL) was developed from the "calculated" RfC ($1,447 \mu\text{g}/\text{m}^3$) by applying a Non-Threshold Effects Uncertainty Factor (NTEUF) of 5 to account for the observed SAR weight-of-evidence. No adjustments were made for multimedia considerations. The resulting NTEL for ethyl benzene was calculated as $289.4 \mu\text{g}/\text{m}^3$ and was then rounded up to $300 \mu\text{g}/\text{m}^3$. The AAL is derived from the TEL or the NTEL, whichever one of these values is lower. Since the TEL and NTEL were equivalent, the value of $300 \mu\text{g}/\text{m}^3$ was adopted by Massachusetts as the AAL for ethyl benzene.

New York based its SGC on the TLV-TWA limit of 100 ppm ($434 \text{ mg}/\text{m}^3$) from the ACGIH for ethyl benzene. The ACGIH reported that transient eye irritation was found in human subjects exposed to 200 ppm ethyl benzene. At 1,000 ppm there was irritation and tearing, and at 2,000 ppm there was immediate severe eye irritation and tearing with moderate nasal irritation (ACGIH, 1991). The ACGIH reports that, following its review of the data, no systemic effects would be expected at concentrations of ethyl benzene which would produce "distinctly disagreeable skin and eye irritation". Accordingly, the ACGIH recommended a TLV-TWA of 100 ppm ($434 \text{ mg}/\text{m}^3$) based on the prevention of "disagreeable irritation" (ACGIH, 1991).

The TLV was adjusted by New York before being applied as an air quality guideline. These adjustments account for the differences from the intended application of the occupational exposure limits, i.e., a healthy adult worker exposed 8 hours/day or 40 hours/week over the course of his or her working life, to a member of the general population (perhaps more sensitive to the effects of a toxic substance) exposed continuously over a lifetime. New York's SGC value of $100 \text{ mg}/\text{m}^3$ was determined simply by applying a factor of 40 hours/168 hours (i.e., divide by 4.2) to the TLV of $434 \text{ mg}/\text{m}^3$, and rounding it off.

The Netherlands have set an emission standard for ethyl benzene to be used for permitting applications, and a MIC based on the Province of Groningen's guideline. The scientific basis for the derivation of these guidelines was not available. The World Health Organization (WHO) has not recommended a guideline value, for Europe for ethyl benzene (except the tentative guideline of 22 mg/m³) and neither have Sweden and the Canadian Federal Government.

The current US EPA classification of ethyl benzene is Group D (not classifiable), based on the weight-of-evidence approach (US EPA, 1998). It is considered not classifiable due to the lack of animal bioassays and epidemiological studies (US EPA, 1998). The International Agency for Research on Cancer (IARC) has not classified the carcinogenicity of ethyl benzene (ARB, 1996). None of the agencies reviewed have based their criteria for ethyl benzene on a carcinogenic endpoint. However, recent findings of the NTP study may raise the possibility that ethyl benzene is an animal carcinogen.

5.0 Responses of Stakeholders to the Information Draft

In January, 1999, the Ministry posted information draft documents for eighteen chemicals, including ethyl benzene, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and any technical or economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received three submissions from stakeholders regarding the draft document for ethyl benzene. A stakeholder from the automotive industry recommended that the Ministry base its AAQC on the RfC from the US EPA but not round this value down to 1,000 µg/m³. The automotive stakeholder also indicated that the POI should remain at current level. An automotive equipment and parts manufacturing stakeholder pointed out that ethyl benzene was a common contaminant of commercial xylene for paint coatings and therefore economic impacts should be examined for a lowered standard. The utility sector indicated that they would not have a problem meeting a lowered standard.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is

now complete. During that initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for ethyl benzene. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard.

7.0 Considerations in the Development of Air Quality Standards for Ethyl Benzene

The existing 24-hour AAQC for ethyl benzene in Ontario is $4000 \mu\text{g}/\text{m}^3$, while the POI standard is $4000 \mu\text{g}/\text{m}^3$. Both values are based on odour as a limiting effect.

The concentrations of ethyl benzene which induce lethality in animals is often above 1000 ppm ($4350 \text{ mg}/\text{m}^3$) in acute or subchronic exposures, and there are apparent differences in species sensitivity. Information on the lethality, or the systemic effects, of ethyl benzene exposure in humans is not sufficient to draw any conclusion because quantitative data on concentration and duration are not always available. Interpretations are often obscured by the existence of confounding factors such as co-exposure with other toxic substances, however, common effects appear to be pulmonary and ocular irritation and possible haematological changes. In animals, NOAEL were identified in a variety of studies for the systemic, immunological, neurological, reproductive and developmental toxicity of ethyl benzene for subchronic/chronic exposures. It is considered that the developmental effects may be the most sensitive endpoint. For example, the NOAEL ranged from 97 ppm or $422 \text{ mg}/\text{m}^3$ for developmental effects in rats to 2400 ppm or $10440 \text{ mg}/\text{m}^3$ for effects on liver, kidney, and the respiratory system in rabbits. The US EPA considers the developmental effects a critical endpoint and hence developed a RfC on this basis.

None of the agencies reviewed appear to consider the carcinogenic potential of ethyl benzene, likely due to the fact that reliable studies were not available at the time when their criteria were established. Recently, the National Toxicology Program (NTP) concluded in a draft report on inhalation carcinogenicity for ethyl benzene, that there was clear evidence of carcinogenic activity of ethyl benzene in male rats and some evidence of carcinogenic activity in female rats as well as in male and female mice. However, the US EPA has not yet provided a cancer risk assessment for ethyl benzene based on the NTP findings.

In the absence of a comprehensive cancer risk assessment for ethyl benzene, the inhalation RfC of $1,000 \mu\text{g}/\text{m}^3$ developed by the US EPA would appear to provide an adequate degree of protection against the most sensitive non-cancer endpoint for this chemical. This view is supported by the fact that all five of the US state agencies reviewed have adopted, or will adopt, this RfC for their ambient air quality criteria. In agreement with these state agencies, the MOE has considered that it is appropriate to use the US EPA RfC of $1,000 \mu\text{g}/\text{m}^3$ as the basis for the derivation of a 24-hour AAQC.

The odour threshold determined by a MOE panel is $1,900 \mu\text{g}/\text{m}^3$ and this value is comparable to those of the health-based exposure limits. In light of this observation, this odour threshold can be used as the 10-minute AAQC.

There is inadequate information concerning the impact of atmospheric ethyl benzene to terrestrial organisms. However, the Ministry does not anticipate adverse impacts to terrestrial organisms due to emissions to air at the levels which are protective of human health.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the RfC from the United States Environmental Protection Agency. This RfC has been employed to derive air quality standards for ethyl benzene. Since the RfC was derived based on a developmental effect endpoint, it will be used as a 24-hour averaging criterion.

The Ministry of the Environment uses a factor of 3 to derive half-hour POI standards and guidelines from criteria based on 24-hour average concentrations. This factor is derived from empirical measurements which ensures that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). The Ministry also considers the odour property of ethyl benzene for air quality standards. The odour threshold (50% detection) of $1,900 \mu\text{g}/\text{m}^3$ will become a 10-minute AAQC. An odour-based POI can be derived by dividing the 10-minute AAQC with an averaging time conversion factor of 1.36 to obtain a value of $1,400 \mu\text{g}/\text{m}^3$ (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for ethyl benzene:

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- a 24-hour average AAQC of 1,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the adverse health effects of this compound;
 - a 10 -minute average AAQC of 1,900 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the odour nuisance of this compound; and,
 - a half-hour average POI standard of 1,400 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl benzene based on the odour nuisance of this compound.

Since ethyl benzene is a commonly used substance in various industries in Ontario, immediate compliance with this proposed POI standard may be difficult for some industries. Stakeholder comments are requested regarding any technical and/or economic impacts that may be encountered as a result of the revised POI standard. The comments received from stakeholders will help to determine whether or not risk management is required and if so, its extent.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;

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3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
 4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the

federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998. <http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for ethyl benzene can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The Reference Concentration (RfC) for ethyl benzene is 1 mg/m³ or 1000 µg/m³. The US EPA has classified ethyl benzene as a group D carcinogen (i.e., not classifiable as to human carcinogenicity). No air concentration guidelines exist for ethyl benzene.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

Key Reference(s):

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6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

Current.

8. Key Risk Assessment Considerations:

The US EPA has established an inhalation RfC of 1 mg/m^3 ($1,000 \text{ }\mu\text{g/m}^3$) for ethyl benzene, derived from studies conducted by Andrew *et al.* (1981) and Hardin *et al.* (1981). The Andrew *et al.* (1981) study was used as the basis of the numerical RfC derivation, therefore details of this study are provided below. In this study, Wistar rats and New Zealand white rabbits were exposed to nominal concentrations of 0, 100 or 1,000 ppm (0, 435 or 4,350 mg/m^3) ethyl benzene for 6-7 hours/day, 7 days/week during gestation days 1-19 (for rats) and 1-24 (for rabbits). A separate group of rats was exposed for 3 weeks prior to mating and exposure was continued through gestation. The pre-gestationally exposed rats were also exposed to 0, 100, or 1,000 ppm (0, 435 or 4,350 mg/m^3). Pregnant animals were sacrificed 1 day prior to term (21 days for rats; 30 days for rabbits) and maternal organs and fetuses were examined for histopathological and physical abnormalities. Rabbits did not exhibit embryotoxicity, fetotoxicity or teratogenicity at either exposure level. No significant incidences of major malformations or minor anomalies were evident in the fetal rabbits of the exposed groups. There was no evidence of maternal toxicity in the rabbits and no evidence of histologic damage in the maternal organs. There was a statistically significant reduction in the number of live rabbits per litter at both exposure levels, but the number of implantations and the number of dead or resorbed kits per litter were not significantly different from the control group. The US EPA concluded that there was no concentration-related intrauterine mortality.

No histopathological changes were evident in the maternal organs examined from rats exposed only during gestation. There was no effect on fertility or other reproductive endpoints. Liver, spleen and kidney weights were significantly increased in pregnant rats in the 1,000 ppm (4,342 mg/m^3) group. Rat fetuses exhibited an increased incidence of supernumerary and rudimentary ribs in the high exposure group, and an elevated incidence of extra ribs was observed in both exposure groups.

The offspring of rats exposed to 1,000 ppm (4,350 mg/m^3) prior to gestation and throughout gestation exhibited an increased incidence of extra ribs. This was not observed in the 100 ppm (435 mg/m^3) group. There was no evidence of an increased incidence of fetuses with rudimentary ribs in either exposed group. Fewer litters were examined in the group exposed prior to and throughout gestation. No fetal toxicity was noted in these animals. Body weights, placental weights and sex ratios were within normal limits. Significant increases in liver and spleen weights were observed in the 1,000 ppm dose group. However, there were no histopathological changes in any of the organs examined. Skeletal variation in the fetuses was seen at both exposure levels in the rats, with the effects in the 1,000 ppm (4,350 mg/m^3) exposure group occurring more frequently than in the 100 ppm (435 mg/m^3) group. The US EPA (1997) cites the effects observed in either dose group as "marginally adverse". Taken together with other mild effects observed at the 1,000 ppm exposure level, the US EPA concluded that 1,000 ppm was the lowest-observable-adverse-effect-level (LOAEL). The lower exposure concentration (435 mg/m^3) was considered to be the no-observed-adverse-effect-level (NOAEL).

In deriving the RfC for ethyl benzene, the US EPA (1998) applied an uncertainty factor (UF) of 300 to the NOAEL of 435 mg/m³ to account for the protection of sensitive individuals (UF=10), to adjust for the absence of multigenerational reproductive and chronic studies (UF=10) and to extrapolate between species (UF=3). The modifying factor applied was 1. No rationale was provided for the modifying factor. The RfC for ethyl benzene was calculated as 1.447 mg/m³, and rounded down to 1 mg/m³:

$$\text{RfC} = 435 \text{ mg/m}^3 / 300 = 1.447 \text{ mg/m}^3 \text{ or } \rightarrow 1 \text{ mg/m}^3$$

Confidence in the principal study, the overall database of toxicological information and the inhalation RfC for ethyl benzene is reported as low. Although the developmental study by Andrew *et al.* was considered to have been well conducted and indicated no adverse effects in either species tested, the study was given a low confidence rating. More information on potential maternal toxicity and other developmental effects may have been elicited by higher exposure concentrations. The database was given a low confidence rating due to a lack of chronic and multigenerational studies. Since the confidence in both the principal study and the database was low, the confidence in the RfC was also considered low.

9. Key Risk Management Considerations:

No information available.

10. Multimedia Considerations of Guidelines:

No adjustment for multimedia exposure is considered in the development of RfCs (for threshold effects) or unit risk values (for non-threshold effects).

11. Other Relevant Factors:

The National Toxicology Program (NTP) has recently completed a 2-year ethyl benzene inhalation study in rats and mice. The draft technical report was reviewed at a meeting of the NTP Board of Scientific Counselor's Technical Reports Review Subcommittee held on December 11, 1996. The final version of this technical report is in press. In this study, groups of 50 male and 50 female F344/N rats and 50 male and 50 female B6C3F₁ mice were exposed to 0, 75, 250 or 750 ppm (0, 332, 1,108, or 3,323 mg/m³) ethyl benzene by inhalation 6 hours per day, 5 days per week for 104 weeks. The study found a significantly greater incidence of renal tubule adenoma and adenoma or carcinoma (combined) in the male rats exposed to 3,323 mg/m³. In male and female rats, the kidneys showed a significant increase in the incidences of renal tubule adenoma and renal tubule hyperplasia at 3,323 mg/m³. Male mice exposed to 3,323 mg/m³ displayed a significant increase in the incidences of alveolar/bronchiolar adenoma and alveolar/bronchiolar adenoma or carcinoma (combined), compared to the concurrent controls, but were within the NTP historical control range. The incidence of alveolar epithelial metaplasia in 3,323 mg/m³ males was significantly greater than that in the chamber controls. In 3,323 mg/m³ females, the incidences of hepatocellular adenoma and hepatocellular adenoma or carcinoma

(combined) were significantly greater than those in the chamber control group, but were within historical control ranges. The incidence of eosinophilic focus in 3,323 mg/m³ females was significantly increased compared to the controls. The study concludes that there was clear evidence of carcinogenic activity of ethyl benzene in male rats, and some evidence of carcinogenic activity in female rats and male and female mice (NTP, 1996). The US EPA's Office of Research and Development has indicated that there are no immediate or foreseeable plans to re-assess the IRIS file on ethyl benzene (US EPA, 1997). The review, when it does occur, will most probably include an independent carcinogenicity assessment (in light of the NTP report) in addition to the RfC derivation based on non-cancer endpoints (US EPA, 1997). This review could potentially provide a cancer Unit Risk Factor or a revised RfC, both of which would impact on the criteria that different agencies have derived based on the current US EPA RfC. It is not currently possible to assess what these impacts may be.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Ethyl benzene (CAS 100-41-4)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California did not identify any specific air quality guideline value for ethyl benzene. In addition, no risk-based concentration limit has been established for ethyl benzene. However, the OEHHA of the California Environmental Protection Agency has recently proposed to adopt the RfC of 1000 $\mu\text{g}/\text{m}^3$ from the US EPA for its chronic inhalation reference exposure level (REL).

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. *Documentation Available:*

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 467-469.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

6. *Peer-Review Process and Public Consultation:*

The Draft Toxic Air Contaminant Identification list is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS, etc.) and additional widely recognised reference texts.

The Reference Concentrations (RfCs), reference exposure levels (RELs) and cancer potency values reported in both the Draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

7. *Status of Guideline:*

Not applicable

8. *Key Risk Assessment Considerations:*

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for ethyl benzene. The State understands and identifies that the US EPA has established a RfC of 1,000 $\mu\text{g}/\text{m}^3$ based on developmental toxicity in rats and rabbits (ARB, 1996). Despite ethyl benzene is not listed under Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996), the State has proposed to adopt the US EPA's RfC.

Ethyl benzene is identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment" which is the State's next step in establishing a potential air quality guideline value (ARB, 1997).

9. *Key Risk Management Considerations:*

Not applicable

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Ethyl benzene is not one of these substances.

11. *Other Relevant Factors:*

Ethyl benzene is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Ethyl benzene (CAS# 100-41-4)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) for ethyl benzene is 300 $\mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The Allowable Ambient Limit (AAL) for ethyl benzene is 300 $\mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. *Status of Guideline(s):*

Current. Guidelines may be updated periodically.

8. *Key Risk Assessment Considerations:*

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for an adverse effect(s), an occupational limit is used to derive the TEL. When a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined by the MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of ethyl benzene, an IRIS RfC of 1.0 mg/m³ was reported. The MDEP, after having reviewed the basis for this RfC, adopted a level of 1.447 mg/m³ for use in the MDEP air guidelines, instead of 1 mg/m³ which was the published RfC. This level of 1.447 mg/m³ (1,447 µg/m³) was calculated by dividing the no-observed-adverse-effect-level (NOAEL) of 435 mg/m³ that was reported for ethyl benzene in IRIS by the uncertainty factor of 300 that was also reported in the same document (MDEP, 1997).

i.e., "Calculated" RfC = NOAEL/UF = 435 mg/m³ / 300 = 1.447 mg/m³ = 1,447 µg/m³

The MDEP considered the "calculated" RfC of 1,447 µg/m³ as the starting point for the TEL derivation. The RfC was divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The TEL was, therefore, calculated as 289.4 µg/m³, and was then rounded up to 300 µg/m³.

Non-Threshold Effects

The MDEP reported that there was insufficient evidence to classify ethyl benzene's carcinogenic and mutagenic potential (MDEP, 1990). However, the MDEP has summarized ethyl benzene's positive results for structure activity relationships (SAR) analysis. The MDEP scores SAR as "positive" if a substance or its metabolites falls into Group C of the United States Food and Drug Administration's (USFDA) 1982 *Toxicological Principles for the Safety Assessment of Direct Food Additive and Color Additives Used in Food* (MDEP, 1990). The USFDA defines Group C as consisting of additives that are unidentifiable or that contain functional groups of high probable toxicity. The Non-Threshold Effect Exposure Limit (NTEL) was developed from the calculated RfC ($1,447 \mu\text{g}/\text{m}^3$) by applying a Non-Threshold Effects Uncertainty Factor (NTEUF). The NTEUF was assigned a value of 5 which accounts for observed SAR weight-of-evidence. No adjustments were made for multimedia considerations. The resulting NTEL for ethyl benzene was calculated as $289.4 \mu\text{g}/\text{m}^3$ and was then rounded up to $300 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Since the TEL and NTEL were equivalent, the TEL concentration and averaging time ($300 \mu\text{g}/\text{m}^3$ averaged over 24 hours) was adopted as the AAL for ethyl benzene.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end-point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

A factor of 20% was applied to the calculated RfC used as the basis of the TEL guideline to allow for contributions from exposure media other than air.

11. Other Relevant Factors:

The MDEP did not directly adopt the RfC reported in IRIS, but rather used the reported NOAEL and reported uncertainty factor to recalculate the RfC.

The MDEP scores SAR as "positive" if a substance or its metabolites falls into Group C of the United States Food and Drug Administration's (USFDA) 1982 *Toxicological Principles for the Safety Assessment of Direct Food Additive and Color Additives Used in Food* (MDEP, 1990). The

USFDA defines Group C as consisting of additives that are unidentifiable or that contain functional groups of high probable toxicity. The primary urinary metabolites of ethyl benzene in humans were found to be mandelic acid (64%), phenylglyoxylic acid (25%) and methylphenylcarbinol, or 1-phenylethanol (5%) following 8-hour inhalation exposures (ACGIH, 1991). Mandelic acid falls into Group C, therefore the SAR for ethyl benzene was scored by the MDEP as positive. However, the USFDA's rationale for scoring SAR information is not sufficiently well described to evaluate its scientific merits.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)
2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)
3. *Guideline Value(s):* The Initial Threshold Screening Level (ITSL) for ethyl benzene is 1,000 mg/m³, with an averaging time of 24 hours.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

US EPA, 1998. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, D.C.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL. Specifically, information from the US EPA's process for the development of reference concentrations (RfCs), upon which the ITSL for ethyl benzene is based, was employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for ethyl benzene was adopted from the RfC developed by the US EPA. The ITSL, which is averaged over 24 hours, equals the inhalation RfC.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey has not set an air quality standard for ethyl benzene (NJDEP, 1997a). However, the State has adopted the United States Environmental Protection Agency's (US EPA) Integrated Risk Information System (IRIS) risk-based inhalation reference concentration (RfC) of 1,000 $\mu\text{g}/\text{m}^3$ for ethyl benzene (NJDEP, 1997b).

4. *Application:*

The BAQEv Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994a).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

Key Reference(s):

US EPA, 1996. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, DC.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The US EPA's RfC, adopted by New Jersey as its RfC, should be used in risk assessments to estimate the public health risks for inhalation of ethyl benzene using the following equation:

$$\text{Hazard Quotient} = C / \text{RfC}$$

where C = maximum annual average ambient air concentration in $\mu\text{g}/\text{m}^3$
 $\text{RfC} = \text{Inhalation RfC} = 1,000 \mu\text{g}/\text{m}^3$

The RfC of $1,000 \mu\text{g}/\text{m}^3$ is adopted from the US EPA's Integrated Risk Information System (IRIS) (please refer to Section 11.1, Federal Government of the United States, for the derivation of the RfC). The maximum annual average ambient air concentrations of pollutants (C) are derived from one of three approaches: an initial risk screening assessment, dispersion modelling or air monitoring programs (NJDEP, 1997b).

Hazard quotients which are less than or equal to one indicate a risk which is considered to be negligible. However, hazard quotients which are greater than one represent risks which are of concern to the State, and will be evaluated and managed on a case by case basis.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. For carcinogens, Unit Risk Factors must be used to calculate inhalation risks, while cancer potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, RfCs must be used for inhalation exposure, and reference doses (RfDs) for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Ethyl benzene (CAS# 100-41-4)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC) for ethyl benzene is 100,000 $\mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) for ethyl benzene is 1,000 $\mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

Key Reference(s):

ACGIH, 1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices 1990-1991. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. *Key Risk Assessment Considerations:*

Ethyl benzene is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC for ethyl benzene was derived from the ACGIH Threshold Limit Value-Time Weighted Average (TLV-TWA) by dividing the TLV-TWA of 435 mg/m³ by a factor of 4.2 and rounding down to 100,000 µg/m³. The factor used above as the divisor to adjust the occupational limit is based on adjusting 8 hours/day, 5 days/week occupational exposure to 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2).

The AGC for ethyl benzene of 1,000 µg/m³ was adopted from the US EPA's Reference Concentration (RfC) reported in the IRIS database.

9. *Key Risk Management Considerations:*

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guideline considers only human exposure to contaminants in air.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*
None.

4. *Application:*
None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No.

23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*
Not applicable.

7. *Status of Guideline:*
Not applicable.

8. *Key Risk Assessment Considerations:*
None.

9. *Key Risk Management Considerations:*
None.

10. *Multimedia Considerations of Guidelines:*
None.

11. *Other Relevant Factors:*
None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)
2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Ethyl benzene is classified as a class 2 gaseous substance (gO.2). This classification imposes an emission standard of 100,000 $\mu\text{g}/\text{m}^3$, given a mass flow rate of 2.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992). The Netherlands has also adopted a Maximum Immissible Concentration (*sic*) (MIC) of 240 $\mu\text{g}/\text{m}^3$, applied as a three-hour emission limit from the regional MIC developed by the province of Groningen. A Target Concentration value has yet to be identified for ethyl benzene.

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long term environmental quality objective which establishes a target value for which emissions of priority substances must be maintained below. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological

literature. This progressive approach will require facility specific emissions to be kept below a limit or a guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance or limit values are either air quality statutory requirements or non statutory regional specific MIC levels.

5. Documentation Available:

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. Peer-Review Process and Public Consultation:

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 100,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 2.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

The regional MIC values applied in the environmental quality objectives program were derived by the Province of Groningen using the occupational hygiene-based national 1982-1983 Maximum Acceptable Concentrations (MACs) adjusted by a modifying factor. A modifying factor of 1,000 is applied for compounds classified by the International Agency for Research on Cancer (IARC) as substances which may have carcinogenic properties, or which have been shown to cause reproductive or developmental effects. A factor of 150 was applied for all other substances. The MACs from which the MICs are derived are occupational exposure limits and the modifying factor of 1,000 is

intended to account for the extrapolation from a 40 hour work week to a continuous 24 hour exposure, and to adjust for exposure to the general population (children, adults and elderly).

9. Key Risk Management Considerations:

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Ethyl benzene (CAS# 100-41-4)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. Chemosphere 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} .

No human health risk assessment has been carried out for ethyl benzene.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Ethyl benzene (CAS # 100-41-4)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. Ethyl benzene has not been assessed or evaluated under the first Priority Substance List (PSL1). It was nominated as a substance for consideration, but was not recommended for evaluation by the Ministers' Expert Advisory Panel under the Second Priority Substance List (PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or <i>Ontario Ministry of Environment and Energy</i>
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences (USA)</i>
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program (USA)</i>
OEHHA	<i>Office of Environmental Health Hazard Assessment (California EPA)</i>
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration (New York State)</i>
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
ETHYL ETHER**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Ethyl ether was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing standard in 1985. A review of the scientific and technical information relevant to setting an ambient air quality standard for ethyl ether has previously been provided to stakeholders for their comments. This document therefore, provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour Point of Impingement (POI) standard for ethyl ether.

Ethyl ether, CAS # 60-29-7, is a clear, volatile liquid with a sweet, pungent odour. It is used as a solvent for waxes, fats, oils, perfumes, alkaloids, and gums. It is a solvent for nitrocellulose when mixed with alcohol. It is an important reagent in organic syntheses, particularly in Grignard and Wurtz type reactions, and is used in the manufacturing of gun powder and as a primer for gasoline engines. Ethyl ether is an easily removable extractant of active principles (hormones, etc.) from animal and plant tissues. It is used therapeutically as an inhalation anaesthetic and antispasmodic.

Ethyl ether can be absorbed through inhalation or ingestion. It is instantly absorbed into the bloodstream once inhaled and then passes quickly into the brain. Ethyl ether is partly metabolized to carbon dioxide and to urinary metabolites, but over 90% is excreted unchanged through exhaled air. A small fraction of unmetabolized ethyl ether is excreted through urine, sweat, milk, and other body fluids, as well as through the intact skin through diffusion. Ethyl ether passes easily through the placental barrier. Narcosis and general anaesthesia are the main physiologic effects following exposure to ethyl ether. Inhalation may cause dizziness, giddiness, euphoria, central nervous system depression, and skin, eye, and mucous membrane irritation. Ethyl ether abuse, or intoxication has been associated with anorexia, albuminuria, nephritis, and occasionally causing death due to respiratory failure. Loss of appetite, exhaustion, headache, sleepiness, excitation, and psychological disturbances are all symptoms resulting from chronic exposure to ethyl ether.

Ethyl ether has not been evaluated by the United States Environmental Protection Agency (US EPA) for evidence of its carcinogenic potential in humans. Furthermore, through the National Toxicology Program, the U.S. Department of Health & Human Services has not conducted carcinogenicity studies on ethyl ether.

Ethyl ether may be released into the environment as a result of its industrial applications. Ethyl ether is not listed in the National Pollutant Release Inventory (NPRI) of Environment Canada for the reporting

of environmental releases. Neither Environment Canada nor the MOE monitor ambient air routinely for ethyl ether. No ambient air concentration data was found for Ontario or Canada.

The current half-hour Point of Impingement (POI) guideline and 24-hour Ambient Air Quality Criterion (AAQC) are set at 30,000 $\mu\text{g}/\text{m}^3$ based on odour and health and odour effects, respectively.

In revising the air quality standards for Ontario, the MOE is reviewing and considering risk assessments, and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, and the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of the Environment and Health Canada.

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry agrees with the states of Massachusetts, Michigan and New York and accepts the scientific studies which support the development of the occupational exposure limit (TLV-TWA) from the American Conference of Governmental Industrial Hygienists. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for ethyl ether based on the rationale of this occupational exposure limit. The Ministry also considers the odour effect of ethyl ether in deriving a POI. An odour detection threshold of 950 $\mu\text{g}/\text{m}^3$ is considered a 10-min AAQC and a half-hour POI can be derived from this 10-min AAQC.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for ethyl ether:

- a 24-hour average AAQC of 8,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether based on the adverse health effects of this compound; and,
- a 10-minute average AAQC of 950 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether based on the odour nuisance of this compound.

Based on supporting science and dispersion modelling, a half-hour POI standard of 700 $\mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of 30,000 $\mu\text{g}/\text{m}^3$ to this revised level of 700 $\mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **700 $\mu\text{g}/\text{m}^3$ to 7000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Ethyl ether was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing standard in 1985. A review of scientific and technical information relevant to setting an ambient air quality standard for ethyl ether had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for ethyl ether.

2.0 General Information

2.1 Physical/Chemical Properties

The following list provides some general information on ethyl ether and its properties:

CAS #	60-29-7
RTECS #	KI5775000
UN #	1155
Conversion Factors	1 ppm = 3.03 mg/m ³ @ 25 °C and 1 atm 1 mg/m ³ = 0.33 ppm @ 25 °C and 1 atm
Boiling Point	34.6 °C @ 760 mm Hg
Flash Point	-45 °C
Henry's Law Constant	1.23 x 10 ⁻³ atm m ³ /mol @ 25 °C
Log K _{ow}	0.89
Formula	C ₄ H ₁₀ O
Molecular Weight	74.14 g/mol
Vapour Density (air = 1)	2.56
Vapour Pressure	442 mm @ 20 °C, 537 mm @ 25 °C
Common Synonyms	Anaesthetic ether, diethyl ether, diethyl oxide, ethoxyethane

Ethyl ether is a clear, volatile liquid with a sweet, pungent odour (Lewis, 1992). It is extremely flammable and a severe fire and explosion hazard when exposed to heat or flame (ACGIH, 1991). Ethyl ether is soluble in water, miscible with the lower aliphatic alcohols, benzene, chloroform, petroleum ether, other fat solvents, and many oils (ACGIH, 1991).

There is a wide range of odour detection thresholds identified in the literature spanning roughly an order of magnitude (Verschuere, 1983; Ruth, 1986). These values range from 700 to 3000 µg/m³, with the majority being around 1000 µg/m³. Odour impact modelling conducted by the MOE that utilized an odour panel, reported a geometric mean value for detection of 950 µg/m³ as a 50% detection level. Due to the range of study design, quality and reporting, the American Industrial Hygiene Association conducted a review of existing compilations of odour criteria and developed a number of conditions for acceptance of an odour impact study (AIHA, 1989). In general, the AIHA recommends that the odour threshold should be established at the geometric mean of the range of values which came from studies meeting the conditions of acceptability.

2.2 Uses

Ethyl ether is widely used as a solvent for waxes, fats, oils, perfumes, alkaloids, and gums (ACGIH, 1991; HSDB, 1997; Windholz *et al.*, 1976). It is also a solvent for nitrocellulose when mixed with alcohol, it is an important reagent in organic syntheses particularly in Grignard and Wurtz type reactions, and is used in the manufacture of gun powder and as a primer for gasoline engines (HSDB, 1997; Windholz *et al.*, 1976). Ethyl ether is used to extract active principles (hormones, etc.) from animal and plant tissues. Other applications include uses in analytical chemistry and as a therapeutic anaesthetic gas (Verschuere, 1983).

2.3 Sources and Levels

Ethyl ether is not on the list of substances subject to reporting on the NPRI of Environment Canada (NPRI, 1996). However, ethyl ether may be released into the environment as a result of its industrial applications. As a result of the widespread use of ethyl ether as a solvent, it is likely released from many facilities in small quantities. For example, the use of ethyl ether in paint and coatings operations would suggest that there would be some releases of ethyl ether to the atmosphere from facilities employing this type of operation.

Neither Environment Canada nor the MOE routinely monitor ambient air for ethyl ether. No ambient air data were found for Ontario or Canada, and no data was located for ambient concentrations of ethyl ether either outdoors or indoors. In the process of reviewing a sample of MOE Certificates of Approval, a median of $75 \mu\text{g}/\text{m}^3$ was indicated for modelled ground level concentrations (GLC) for various industries. The GLCs ranged from a low of $0.936 \mu\text{g}/\text{m}^3$ to a high of $7619 \mu\text{g}/\text{m}^3$ (MOE, 1998).

2.4 Environmental Fate

Due to the volatile nature of ethyl ether, most releases of this chemical will ultimately end up in the atmosphere. It will undergo photo-oxidation by reacting with photochemically produced hydroxy radicals. An estimated half-life for this process is 29 hours, which occurs at an atmospheric concentration of 5×10^5 hydroxyl radicals/ cm^3 (HSDB, 1997). Direct photolysis is unlikely to be an important removal process as ethyl ether does not absorb light at wavelengths greater than 290 nm (HSDB, 1997).

Releases of ethyl ether to water are not expected to significantly accumulate in sediments, bioconcentrate in aquatic organisms or hydrolyze. A bioconcentration factor of 2.8 has been estimated for ethyl ether in aquatic organisms, which is based on its octanol-water partitioning coefficient (HSDB, 1997). Ethyl ether is expected to be very mobile in soil and may leach through soil into groundwater

(HSDB, 1997). Experiments utilizing activated sewage sludge indicated that ethyl ether is resistant to biodegradation in environmental media (HSDB, 1997).

3.0 Toxicology of Ethyl Ether

The following toxicological review of ethyl ether is primarily focussed on the inhalation route of exposure, as this is the predominant pathway of human exposure, which is due to the volatile nature of this compound. Data on other exposure media are included where relevant, or where inhalation data are lacking.

Ethyl ether can be absorbed through inhalation or ingestion (Elvestad et al., 1993). Ethyl ether is instantly absorbed, into the bloodstream, once inhaled and then passes quickly into the brain. Once absorbed, ethyl ether rapidly accumulates in fatty tissue and the brain (HSDB, 1997). High levels of ethyl ether have also been reported in fatty tissue of dogs after 2.5 hours of anaesthesia, and unexplained high concentrations have been found in the adrenals during anaesthesia. Approximately 8-10% of absorbed ethyl ether is metabolized in the body, with the majority excreted unchanged via the lungs (NEG/NIOSH, 1993). Ethyl ether is partly metabolized to carbon dioxide and to urinary metabolites, however over 90% is excreted unchanged through exhaled air. A small fraction of unmetabolized ethyl ether is excreted through urine, sweat, milk, other body fluids, and through the intact skin by diffusion. Ethyl ether easily passes through the placental barrier (HSDB, 1997). [¹⁴C]Ethyl ether administered to mice was metabolized rapidly into palmitic, stearic, and oleic acids, cholesterol, and mono-, di-, and tri-glycerides in the liver (HSDB, 1997).

3.1 Acute Toxicity-Inhalation

Narcosis and general anaesthesia are the main physiologic effects of acute ethyl ether exposure (ACGIH, 1991). Inhalation may cause dizziness, giddiness, euphoria, central nervous system depression, skin, eye, and mucous membrane irritation. Other symptoms include excess salivation, lowered heartbeat, coughing and laryngeal spasm, exhaustion, excitation, headache, seizures and, rarely, death (NIOSH 1994). When used as an anaesthetic, ethyl ether causes mild liver changes for a short duration. However, hepatotoxicity is more likely in patients with pre-existing hepatic injury (HSDB, 1997).

3.2 Subchronic/Chronic Toxicity-inhalation

In humans, chronic ethyl ether abuse or intoxication has been associated with anorexia, albuminuria, nephritis, and occasionally causing death due to respiratory failure (HSDB, 1997). Loss of appetite, exhaustion, headache, sleepiness, excitation, and psychic disturbances are all symptoms resulting from

chronic exposure to ethyl ether (ACGIH, 1991). Dizziness may result from continued inhalation of 2,000 ppm in humans (HSDB, 1997). Albuminuria and polycythemia may also occur (ACGIH, 1991; HSDB, 1997). Prolonged exposures to high vapour concentrations can cause eye injury.

Nelson *et al.* (1943) studied the irritating effects of various solvent vapours on humans. Subject groups reported complaints of nasal irritation starting at 200 ppm (616 mg/m³) and 300 ppm (909 mg/m³) was found objectionable as a working atmosphere. Amor (1950) considered a concentration of ethyl ether, in the atmosphere greater than 500 ppm (1540 mg/m³) as being indicative of unsatisfactory conditions. Henderson and Haggard (1943) concluded that continuous inhalation of 2000 ppm of ethyl ether would probably induce dizziness in some individuals.

Reliable inhalation dose-response studies for ethyl ether are not available. In an oral animal study, four groups of rats were exposed to ethyl ether by gavage at 0, 500, 2,000, and 3,500 mg/kg daily for 13 weeks (US EPA, 1997). Toxicity resulting from the highest dose level included mortality, decreased food consumption, and decreased body weight, which was only significant in the females. No histopathological effects on tissues were observed. Based on this study, the no-observed-adverse-effect-level (NOAEL) is considered to be 500 mg/kg/day and the lowest-observed-adverse-effect-level (LOAEL) is 2,000 mg/kg/day, which results in a significant depression in body weight in male rats (US EPA, 1997).

3.3 Developmental/Reproductive Toxicity

Data regarding the developmental/reproductive effects of ethyl ether are limited. Taskinen, *et al.* (1994) carried out a retrospective case-control study of pregnancy outcomes among laboratory workers, with multiple chemical exposures in Finland occurring between 1973 and 1996. It was found that spontaneous abortion, congenital malformation or low birth weight in the exposed women workers were not statistically significant compared to those who were not exposed to ethyl ether. In an animal study, some embryo toxic and teratogenic effects were noted when ethyl ether was used in anaesthesia on pregnant mice and rats. However, the authors did not consider ethyl ether to be "highly teratogenic" (US EPA, 1997).

3.4 Genotoxicity

Ethyl ether was found to be non-mutagenic in a forward gene mutation assay in *Aspergillus nidulans* and a sperm morphology assay in mice (GENETOX, 1997). An *in vitro* sister-chromatid exchange study (cell type listed as non-human) and an Ames assay (in *Salmonella typhimurium*) both yielded inconclusive results. The only positive mutagenicity result was for a bacterial DNA repair assay in *Escherichia coli* (GENETOX, 1997).

3.5 Carcinogenicity

Ethyl ether has not been evaluated by the United States Environmental Protection Agency (US EPA) for evidence of its carcinogenic potential in humans (US EPA, 1997). The US National Toxicology Program has not conducted carcinogenicity studies on ethyl ether (ACGIH, 1991). The International Agency for Research on Cancer (IARC, 1976) made a reference to ethyl ether in the evaluation of inhalation volatile anaesthetics as a class, however, no information on the carcinogenicity of ethyl ether was presented. No data are cited in the NEG/NIOSH (1993) review, which would indicate any mutagenic or carcinogenic potential for this substance.

3.6 Environmental Effects

There are very limited environmental effect data for ethyl ether. Data for terrestrial wildlife are not available. A 96-hour LC_{50} value of 2,560 mg/L was determined for fathead minnow (*Pimephales promelas*) exposure to ethyl ether (Geiger et al, 1986).

4.0 Review of Existing Air Quality Regulations

4.1 Overview

Ontario currently has an AAQC for ethyl ether. The half-hour POI guideline and 24-hour AAQC are both set at 30,000 $\mu\text{g}/\text{m}^3$, and were established on the basis of a review of health effects conducted in 1985 (MOEE, 1994).

The documentation from ten other agencies (the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government) were reviewed for the existence and basis of air quality criteria for ethyl ether. A brief summary of this review is presented in Table 1 and agency-specific summaries of information concerning air quality guidelines for ethyl ether are presented in Section 11.0 of the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE typically uses a factor of 15 to convert from guidelines based on annual average concentrations to half-hour point-of-impingement limits, and a factor of 3 to convert from guidelines based on 24-hour average concentrations (MOE, 1987; MOEE, 1994b). These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality

guidelines based on longer-term exposures will not be exceeded. However, depending on the health end-point being considered, other conversion factors may also be employed.

Of the agencies reviewed, three jurisdictions, the States of Michigan, New York and the Commonwealth of Massachusetts have developed criteria for ethyl ether. No US EPA reference concentration (RfC) for ethyl ether is currently available. A risk assessment for ethyl ether is under review by a US EPA working group (US EPA, 1997). The States of Michigan, New York and the Commonwealth of Massachusetts have based their criteria, for ethyl ether on the ACGIH TLV- TWA. Based on the annual average, these criteria range from a high of 29,000 $\mu\text{g}/\text{m}^3$ to a low of 164.9 $\mu\text{g}/\text{m}^3$. The difference in criteria are due to the varying policies with regards to derivation of ambient air guidelines from occupational exposure values. The ACGIH (1991) recommends a TLV-TWA of 400 ppm (1,210, 000 $\mu\text{g}/\text{m}^3$) for ethyl ether.

The Netherlands have set an emission standard for ethyl ether which is used for permitting, an application which is not consistent with the intended application in Ontario. California, New Jersey, the WHO, Sweden and the Canadian Federal Government have not established air quality guidelines for ethyl ether.

Table 1. Summary of Existing Air Quality Guidelines^[1] for Ethyl Ether

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration): none.			
California	None.			
Massachusetts	TEL (Threshold Effects Exposure Limits): 329.80 $\mu\text{g}/\text{m}^3$ (24-hour average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 164.90 $\mu\text{g}/\text{m}^3$ (annual average).	TLV-TWA from ACGIH.	1995	
Michigan	ITSL (Initial Threshold Screening Level): 12,000 $\mu\text{g}/\text{m}^3$ (8-hour average).	TLV-TWA from ACGIH.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	None.			
New York State	SGC (Short-Term Guideline Concentration; 1-hour): 290,000 $\mu\text{g}/\text{m}^3$.	TLV-TWA from ACGIH.	1995	Used for permitting.
	AGC (Annual Guideline Concentration): 29,000 $\mu\text{g}/\text{m}^3$.		1995	Used for permitting.
WHO	None.			
Netherlands	150,000 $\mu\text{g}/\text{m}^3$ (half-hour average).	Emission standard.	1992	Used for permitting.
Sweden	None.			
CEPA	None.			
Ontario	half-hour POI guideline: 30,000 $\mu\text{g}/\text{m}^3$.	Health effects.	1985	POI guideline
	24-hour AAQC: 30,000 $\mu\text{g}/\text{m}^3$.	Odour and health effects.		

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed (in the case where no RfC has been developed).

4.2 Evaluation of Existing Criteria

The States of Michigan and New York and the Commonwealth of Massachusetts derived their criteria for ethyl ether based on occupational exposure limits. In the process of derivation, specific uncertainty factors were applied by the respective agencies to the ACGIH's TLV-TWA of 400 ppm or 1,210 mg/m³ (ACGIH, 1991). The ACGIH also has set a short-term excursion limit (STEL) of 500 ppm (1520 mg/m³). ACGIH indicates that these concentrations "should minimize the potential for demonstrable injury to health, irritation or signs of narcosis among exposed workers".

The rationale for the established TLV-TWA value by the ACGIH is not explained in detail, however it seems to be derived from the studies of Amor (1950) and Cook (1945) that unsatisfactory exposure conditions and demonstrable injury to health as well as irritation would not occur if exposed at or below 500 ppm (1520 mg/m³). This was supported by the study of Henderson and Haggard (1943) who estimated that a 70-kg man inhaling 400 ppm could absorb a maximum of 1.25 g of ethyl ether and the resultant blood concentration would not be associated with any signs of intoxication. The ACGIH also discusses the studies conducted by Nelson *et al.* (1943), in which complaints in human subjects began at 200 ppm (606 mg/m³). A concentration of 300 ppm (909 mg/m³) was considered an objectionable working atmosphere. This study clearly indicates that nasal irritation can occur at concentrations well below the TLV-TWA limit. The NIOSH (1994) has questioned the adequacy of the TLV-TWA of the ACGIH for protecting workers. In general, it is clear that ocular and nasal irritation are the critical effects of ethyl ether exposure in humans, and that these effects can be expected to occur at levels between 200 ppm and 400 ppm (606-1212 mg/m³).

When employing occupational exposure limits for the derivation of environmental criteria, uncertainty factors are often applied to provide a sufficient margin of safety for the protection of health. The State of Michigan utilized an uncertainty factor of 100 in the derivation of its Initial Threshold Screening Level (ITSL; 12,000 µg/m³; 8-hour average). A factor of 10 was used to account for differences between work exposure (40 hour week, 30 years) and continuous lifetime exposures, and a factor of 10 for differences in susceptibility between the healthy adult worker population as compared to the general population.

New York State used a factor of 4.2 to account for continuous exposure for its Short-term Guideline Concentration (SGC; 290,000 µg/m³; 1-hour average). New York State also derived its annual criterion from the TLV-TWA. Since ethyl ether is considered of low toxicity, New York State only applied an additional factor of 10 to account for variations in the sensitivity of individuals to ethyl ether in the derivation of its annual guideline concentration of 29,000 µg/m³ based on the SGC.

Massachusetts applied a total uncertainty factor of 3,675 to derive its 24-hour TEL of 329.8 µg/m³. This factor was obtained from dividing the TLV-TWA of 1210 mg/m³ by 4.2 to account for continuous

exposure, 1.75 to account for differences in sensitivity between adults and children, 10 to account for high-risk groups, and a factor of 10 to account for incomplete data. This gave a value of 1,648.98 $\mu\text{g}/\text{m}^3$ as an adjusted Most Appropriate Occupational Limit (MOAL). The MOAL was further adjusted by an additional factor of 5 for potential exposure through routes other than air. In view of the relatively low toxicity of ethyl ether, the factor of 10 for incomplete database would appear to be excessive. As well, most of the emitted ethyl ether is likely to be found in the air and inhalation is likely the primary route of human exposure, therefore the additional factor of 5 for exposure through routes other than air would appear to be unnecessary.

Massachusetts also derived its annual criterion on the basis of the TLV-TWA. Massachusetts adjusted MAOL of 1,648.98 $\mu\text{g}/\text{m}^3$ by a factor of 10 to derive a non-threshold effects level of 164.9 $\mu\text{g}/\text{m}^3$. Since this is lower than the threshold effect level, 164.9 $\mu\text{g}/\text{m}^3$ was adopted as the annual average criterion. The factor of 10 was to take into the mutagenic potential in the absence of carcinogenic data and negative SAR analysis.

Massachusetts' guidelines may have been overly conservative in its choice of uncertainty factors. The factors used by New York State may have underestimated the potential adverse central nervous system effects of ethyl ether. Neither the agencies of New York or Michigan appeared to have considered that ocular and nasal irritation effects had been observed at levels equivalent to, or below the TLV-TWA of 1210 mg/m^3 .

It should be noted that the criteria of the states of Michigan and New York are much higher than the reported odour thresholds of 700 - 3000 $\mu\text{g}/\text{m}^3$.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including ethyl ether, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and any technical and economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period no comments were received regarding risk assessments specific to ethyl ether from the industrial sectors or the general public.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for ethyl ether. If the proposed standard cannot be met immediately this phase will be followed by a third phase in which risk management is discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised odour-based values and the current standard, an interim standard may be warranted depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for Ethyl ether

The existing AAQC and the half-hour POI guideline for ethyl ether are both set at $30,000 \mu\text{g}/\text{m}^3$. These criteria were established based on the odour and health and odour effects of this compound, respectively.

Inhalation exposure to ethyl ether may induce adverse effects on the central nervous system. These effects range from narcosis and general anaesthesia to dizziness and ocular and nasal irritation. Since ethyl ether is a commonly used industrial solvent, the ACGIH has developed occupational exposure limits to protect the worker from the adverse effects of ethyl ether. Three of the ten agencies reviewed have derived air quality criteria from the TLV-TWA of $1210 \text{ mg}/\text{m}^3$ (400 ppm) from the ACGIH. However, ethyl ether induced ocular and nasal irritation in humans at $616 \text{ mg}/\text{m}^3$ (200 ppm) and at $909 \text{ mg}/\text{m}^3$ (300 ppm) may provide an objectionable working atmosphere.

Ethyl ether has a pungent odour and the detection threshold range from $700 - 3000 \mu\text{g}/\text{m}^3$. Based on an odour impact model, the MOE reported an odour threshold (50% detection) of $950 \mu\text{g}/\text{m}^3$. The aesthetic effect of ethyl ether is a critical effect to be considered in the development of air quality

standards for Ontario. A 10-minute average AAQC is usually based on the best estimate of the odour threshold, which in this case is $950 \mu\text{g}/\text{m}^3$.

There are insufficient data to establish an air criterion based on the effects of ethyl ether on vegetation. However, at concentrations below the proposed criteria ethyl ether is not expected to have any adverse effects on plants or other terrestrial organisms.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry agrees with the states of Massachusetts, Michigan and New York and accepted the scientific studies which support the development of the occupational exposure limit (TLV-TWA) from the ACGIH. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for ethyl ether based on the rationale for this occupational exposure limit. The TLV-TWA of $1210 \text{ mg}/\text{m}^3$ is divided by a factor of 1.5 to convert from an 8-hour work day exposure to a 24-hour equivalent averaging time (MOE, 1987). An uncertainty factor of 10 is applied because the exposure limit was based on an observable adverse effect level (LOAEL), rather than a no-observable adverse effect level (NOAEL) and that ocular and nasal irritation may occur at a concentration below the TLV-TWA. Another uncertainty factor of 10 is used for the protection of sensitive individuals (total uncertainty factor of 150). As a result, a 24-hour AAQC of $8,000 \mu\text{g}/\text{m}^3$ can be derived.

The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). On this basis, a half-hour POI value of $24,000 \mu\text{g}/\text{m}^3$ can be estimated. As well, the Ministry also considers the odour property of ethyl ether a critical factor for air quality standard development. In view of the odour property of this compound, a 10-minute AAQC of $950 \mu\text{g}/\text{m}^3$ can be established. Applying the averaging time conversion method mentioned above, a POI value of $700 \mu\text{g}/\text{m}^3$ can be obtained by dividing the 10-minute AAQC of $950 \mu\text{g}/\text{m}^3$ by a factor of 1.36.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for ethyl ether:

- a 24-hour average AAQC of $8,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether based on the adverse health effects of this compound; and,

-
- **a 10-minute average AAQC of 950 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether based on the odour nuisance of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of 700 $\mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of 30,000 $\mu\text{g}/\text{m}^3$ to this revised level of 700 $\mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **700 $\mu\text{g}/\text{m}^3$ to 7000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for ethyl ether.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

-
1. The operations or processes which give rise to emissions of the substance(s) under review;
 2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
 3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
 4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance

based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998. <http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for ethyl ether can be sent to:

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NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS# 60-29-7)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

A chronic inhalation Reference Concentration (RfC) for ethyl ether is not currently available (US EPA, 1997). The US EPA has not evaluated ethyl ether for its human carcinogenic potential (US EPA, 1997). No air concentration guidelines exist for ethyl ether.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

No air concentration guideline exists.

8. *Key Risk Assessment Considerations:*

No information available.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No adjustment for multimedia exposure is considered in the development exposure concentrations for threshold effects or unit risk values for non-threshold effects.

11. *Other Relevant Factors:*

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for ethyl ether. In addition, no risk-based concentration limit has been established for ethyl ether.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. *Documentation Available:*

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

6. *Peer-Review Process and Public Consultation:*

The Draft Toxic Air Contaminant Identification list is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS etc.) and additional widely recognised reference texts.

The Reference Concentrations (RfCs), reference exposure levels (RELs) and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

7. *Status of Guideline:*

Not applicable

8. *Key Risk Assessment Considerations:*

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for ethyl ether. Ethyl ether is not listed under Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996).

Ethyl ether is not identified on the June 1996 Toxic Air Contaminants Identification List (ARB, 1997).

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Ethyl ether is not one of these substances.

11. *Other Relevant Factors:*

None.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Ethyl ether (Ether) (CAS# 60-29-7)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) is 329.80 $\mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The allowable ambient limit (AAL) is 164.90 $\mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1987. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from

the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of ethyl ether, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH Threshold Limit Value - Time Weighted Average (TLV-TWA) occupational exposure limit for ethyl ether, has adopted the level of 400 ppm (equivalent to 1,212 mg/m³, assuming 25°C, 1 atmosphere, and molecular weight of 74.1 g/mol). This level was considered the Most Appropriate Occupational Limit (MAOL) for use in the MDEP air guidelines and was adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week, to consider continuous exposure.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 10 to account for incomplete data in the toxicity database used to review the potential toxicity of ethyl ether.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, 735. The adjusted MAOL is numerically equivalent to 1,648.98 µg/m³. At this point, another set of uncertainty factors were applied to the adjusted MAOL:

-
- I. divided by 1. The Threshold Effects Uncertainty Factor (TEUF) is an uncertainty factor which accounts for acute, chronic, developmental or reproductive effects that may not have been considered in the health risk assessment of the occupational limit. The MDEP applied a score of 1 for ethyl ether.
 - II. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 3,675. The TEL was, therefore, calculated as $329.80 \mu\text{g}/\text{m}^3$.

Non-Threshold Effects

The MDEP reported that there was limited evidence to classify ethyl ether's mutagenic potential based on one positive result as the weight-of-evidence for mutagenicity. There was inadequate or no data to classify ethyl ether's carcinogenic potential (MDEP, 1990) and a negative result for ethyl ether's structure activity relationship (SAR) analysis. The Non-threshold Effect Exposure Limit (NTEL) was developed from the adjusted MAOL ($1,648.98 \mu\text{g}/\text{m}^3$) using a Non-Threshold Effects Uncertainty Factor (NTEUF) of 10. The NTEUF accounts for the mutagenic potential in the absence of carcinogenic data and negative SAR analysis. No adjustment was made for multimedia considerations. The resulting NTEL for ethyl ether was calculated as $164.9 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the NTEL for ethyl ether of $164.9 \mu\text{g}/\text{m}^3$ was adopted as the AAL.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)
2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)
3. *Guideline Value(s):* The Initial Threshold Screening Level (ITSL) is 12,000 mg/m³, averaged over 8 hours.
4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

 - i) each source must apply the best available control technology for toxics (T-BACT);
 - ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices. Sixth Edition. American Conference of Governmental Industrial Hygienists Inc. Cincinnati, Ohio.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL. Specifically, information from the American Conference of Governmental Industrial Hygienist's (ACGIH) process for development of Threshold Limit Values (TLVs), upon which the ITSL for ethyl ether is based, were employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for ethyl ether was determined from the TLV-Time Weighted Average (TLV-TWA) established by the ACGIH and has an averaging time of 8 hours. The ITSL was determined by dividing the occupational exposure level (OEL) (in this case, the ACGIH TLV-TWA) by 100. The 100 fold factor was derived as follows:

$$\text{ITSL} = \text{OEL} \times \frac{40 \text{ hours}}{168 \text{ hours}} (\text{A}) \times \frac{30 \text{ years}}{70 \text{ years}} (\text{B}) \times \frac{1}{10} (\text{C}) = \frac{\text{OEL}}{100}$$

where:

A adjusts for the difference between a 40 hour work week and the total hours in a week;

B adjusts for the difference between the number of years a person is assumed to work and the assumed lifetime;

C adjusts for the possible higher susceptibility of certain individuals in the general population when compared to healthy adult workers.

With a conversion factor of $1 \text{ ppm} = 3.03 \text{ mg/m}^3$, 400 ppm is equivalent to $1,210 \text{ mg/m}^3$ or $1,210,000 \text{ mg/m}^3$. This was divided by 100 and rounded down to arrive at the ITSL of $12,000 \text{ mg/m}^3$.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of the Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey does not set air quality standards (NJDEP, 1997). The State has not identified any risk-based concentration limit for ethyl ether.

4. *Application:*

The Bureau of Air Quality Evaluation (BAQEv) Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEPa, 1994).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. URFs must be used to calculate inhalation risks for carcinogens, while cancer potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, reference concentrations (RfCs) must be used for inhalation exposure, and reference doses (RfDs) for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS# 60-29-7)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC) for ethyl ether is 290,000 $\mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) for ethyl ether is 29,000 $\mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices, Sixth Edition. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. Key Risk Assessment Considerations:

Ethyl ether is classified as a low toxicity air contaminant (Table IV, Appendix C of NYSDEC, 1991). Low toxicity air contaminants are defined as those chemicals for which irritation is the primary toxicological concern.

The SGC was derived from ACGIH Threshold Limit Value-Time Weighted Average (TLV-TWA) (1991) by dividing the ACGIH TLV-TWA ($1,210 \text{ mg/m}^3$) by 4.2 and rounding up to $290,000 \text{ } \mu\text{g/m}^3$. The AGC was derived from the same ACGIH TLV-TWA (1991) by dividing the TLV by 42 and rounding up to $29,000 \text{ } \mu\text{g/m}^3$.

$$\text{SGC} = 1,210 \text{ mg/m}^3 / 4.2 = 288 \text{ mg/m}^3 = 290,000 \text{ } \mu\text{g/m}^3 \text{ (approximately)}$$

$$\text{AGC} = 1,210 \text{ mg/m}^3 / 42 = 28.8 \text{ mg/m}^3 = 29,000 \text{ } \mu\text{g/m}^3 \text{ (approximately)}$$

The factor used above as the divisor in developing the SGC to adjust the occupational limit is based on adjusting 8 hour/day, 5 days/week occupational exposure to 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2). To compensate for applying occupational guidelines to the general population in establishing an AGC, an additional factor of 10 is used for contaminants defined as low toxicity chemicals (a factor of 100 is used for contaminants defined as moderate toxicity chemicals).

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. Multimedia Considerations of Guidelines:

The NYSDEC guideline considers only human exposure to contaminants in air.

11. Other Relevant Factors:

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*
None.

4. *Application:*
None.

5. *Documentation Available:*
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23.
World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*
Not applicable.

7. *Status of Guideline:*
Not applicable.

8. *Key Risk Assessment Considerations:*
None.

9. *Key Risk Management Considerations:*
None.

10. *Multimedia Considerations of Guidelines:*
None.

11. *Other Relevant Factors:*
None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Ethyl ether is classified as a class 3 gaseous substance (gO.3). This classification imposes an emission standard of 150,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 3.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long-term environmental quality objective which establishes a target value below which emissions of priority substances must be maintained. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological literature. This progressive approach will require facility-specific emissions to be kept below a limit or guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance

or limit values are either air quality statutory requirements or non statutory regional-specific maximum immissible concentration (MIC) levels.

5. Documentation Available:

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven,

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague.

6. Peer-Review Process and Public Consultation:

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 150,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 3.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

9. Key Risk Management Considerations:

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS# 60-29-7)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. Chemosphere 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} . No assessment has been carried out for ethyl ether.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Ethyl Ether (Ether) (CAS # 60-29-7)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. Ethyl ether has not been assessed or evaluated under the first Priority Substance List (PSL1) and is not listed for evaluation under the Second Priority Substance List (PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, October 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either ' <i>Reference Exposure Level</i> ' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or ' <i>Recommended Exposure Limit</i> ' used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV *Threshold Limit Value* - an exposure concentration that should not induce an adverse effect in a work environment

TWA *Time-Weighted-Average* - allowable exposure averaged over an 8-hour workday or 40-hour work week

US EPA *United States Environmental Protection Agency*

WHO *World Health Organization*

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
n-HEPTANE**

February 2000

Standards Development Branch
Ontario Ministry of the Environment



Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which new standards will be developed or current air standards will be reviewed over the next several years. *n*-Heptane was identified as a priority compound for the development of a new air standard based on its pattern of use in Ontario and its adverse health effects. A review of scientific and technical information relevant to setting an air quality standard for *n*-heptane has previously been provided to stakeholders for comment. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for *n*-heptane.

Heptane is a colourless, volatile, flammable liquid with nine isomers, the most common being *n*-heptane. *n*-Heptane has a paraffinic odour. It is employed in organic synthesis, and is an ingredient in gasoline, rubber solvents, naphtha, and other petroleum solvents that are used as fuels and solvents. It occurs in the atmosphere almost entirely in the vapour phase where it is degraded primarily by reacting with photochemically-produced hydroxyl radicals.

The primary health concern associated with *n*-heptane is its depressant effect on the central nervous system. Data from volunteer studies indicated that short-term (a few minutes) exposure to *n*-heptane at about 20,000 mg/m³ resulted in vertigo and incoordination. Exposure to *n*-heptane up to 77,710 mg/m³ for less than 40 minutes induced prostration and loss of reflexes prior to convulsion and death. There is no sufficient information to assess the toxic effects of *n*-heptane in chronic exposures. Studies in animals suggest that *n*-heptane does not possess the neuropathological effects as those exhibited by *n*-hexane.

Data from Environment Canada indicate that the average ambient air concentration for *n*-heptane in Ontario between 1988 and 1995 was 0.81 µg/m³; the maximum level was 87 µg/m³. Data from some U.S. states indicate that atmospheric concentrations of *n*-heptane ranged from 0.008 to 207 µg/m³.

Ontario does not currently have either an ambient air quality criterion or a point of impingement standard for *n*-heptane. In developing the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the U.S. EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Of the jurisdictions examined only the states of Michigan and New York have developed air quality guidelines specifically for *n*-heptane. The guidelines of these agencies were derived from an occupational exposure standard

developed by the National Institute for Occupational Safety and Health (NIOSH) of the U.S. After an evaluation of available toxicological information and occupational exposure limits, the Ministry considers the occupational exposure limit of 1,640 mg/m³ developed by the American Conference of Governmental Industrial Hygienists (ACGIH) reasonable. The Ministry considers the application of an uncertainty factor of 100 appropriate to avoid the adverse health effects of *n*-heptane from environmental exposures. Applying the uncertainty factor to the TLV-TWA and the conversion of the occupational exposure period to a 24-hour averaging exposure period results in a 24-hour AAQC of 11,000 µg/m³.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria and half-hour Point Of Impingement standard for *n*-heptane:

- a 24-hour average AAQC of 11,000 µg/m³ (micrograms per cubic metre of air) for *n*-heptane based on the adverse health effects of this compound; and,
- a half-hour POI standard of 33,000 µg/m³ (micrograms per cubic metre of air) *n*-heptane based on the adverse health effects of this compound.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

n-Heptane was identified as a priority for the development of a new air standard based on its pattern of use in Ontario and the toxicological information for this compound. A review of scientific and technical information relevant to setting an ambient air quality standard for *n*-heptane had been provided in a previous document for stakeholder comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour point of impingement (POI) standard for *n*-heptane.

2.0 General Information

2.1 Physical/chemical Properties

The following list provides some general information on *n*-heptane and its properties:

CAS #	142-82-5
RTECS #	MI7700000
UN #	1206
Conversion Factors	1 ppm = 4.09 mg/m ³ @ 25 °C and 760 mm Hg 1 mg/m ³ = 0.245 ppm @ 25 °C and 760 mm Hg
Boiling Point	98 °C
Henry's Law Constant	2.06 atm·m ³ /mole @ 25 °C
Flash Point	-4.4 °C
Log K _{OW}	4.66
Formula	C ₇ H ₁₆
Molecular Weight	100.2 g/mol
Vapour Density (air = 1)	3.52
Vapour Pressure	47.7 mm @ 25 °C
Common Synonyms	heptane, heptyl hydride, Skellysolve C

n-Heptane (C₇H₁₆) is a colourless, volatile, flammable liquid with nine isomers, *n*-heptane being the most common form used in industry. For *n*-heptane the Chemical Abstracts Service (CAS) identification number is 142-82-5, the Registry of Toxic Effects of Chemical Substances (RTECS) number is M17700000 and the United Nations Hazardous Material number is UN1206. It is insoluble in water. *n*-Heptane has a weak, paraffinic odour with a reported odour threshold of 150 ppm (614 mg/m³) (ACGIH, 1991).

2.2 Uses of *n*-Heptane

n-Heptane is employed in organic synthesis and is an ingredient of gasoline and aviation fuel where it is used as a "knock" test standard. It is also used as an ingredient in petroleum naphtha, rubber solvent and other petroleum solvents in glues, varnishes, cements and inks (ACGIH, 1991; Low *et al.*, 1987).

2.3 Sources and Levels

In the atmosphere, *n*-heptane is expected to occur almost entirely in the vapour phase after it is released from the use or disposal of industrial solvents or fuels. The reaction with photochemically-produced hydroxyl radicals in the air is the primary degradation pathway. The estimated half-life in air is 2.2 days at 26°C. Small amounts of *n*-heptane may be removed from the atmosphere by rain washout; however, it would rapidly re-volatilize, according to its Henry's Law constant. *n*-Heptane is not expected to be removed by reacting with ozone, or by direct photochemical degradation, in any significant way (U.S. EPA, 1989).

n-Heptane is not listed as a candidate pollutant on Environment Canada's National Pollutant Release Inventory for environmental release reporting by the industries (NPRI, 1997). In Ontario, ambient air concentrations of *n*-heptane between 1988 and 1995 ranged from zero (below detection limit) to 87 µg/m³. Ninety-nine percent of the observations were below 6.6 µg/m³. The average concentration at a conservation authority was 0.25 µg/m³ while the averages in the urban areas ranged from about 1 µg/m³ to 2.5 µg/m³ (Environment Canada, 1997).

Data from some locations in the U.S.A. indicate that there are apparent variations in the atmospheric concentrations of *n*-heptane in different states, particularly when comparing rural and urban areas (HSDB, 1997). In urban areas throughout the U.S.A., average ground level concentrations (GLCs) varied. For example: in New York City in 1978, the average GLC was 18 ppb (74 µg/m³); GLCs ranged from 3 - 11 ppb (12 - 45 µg/m³) in downtown Los Angeles, California, in a 1981 survey; and in Houston, Texas in 1977, the average concentration was 5 ppb (20.5 µg/m³). In Colorado, GLCs of *n*-heptane ranged from 0.002 - 50.7 ppb (0.008 - 207 µg/m³) with rural areas surrounding Boulder reporting a GLC of 1 µg/m. The ground level concentrations downwind near an automotive plant in Wisconsin ranged from 1 - 1.5 µg/m³.

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 5 facilities with emissions of *n*-heptane covered by a Certificate, were identified. These approvals included emissions from a variety of industries such as, chemical products, coatings and bonding. Currently, Ontario does not have an ambient air quality criterion for this compound. Hence, the applications for a Certificate were reviewed on a case by case basis. The median Ground Level Concentration, estimated by Regulation 346 dispersion modelling for all 5 sources, was approximately 82 µg/m³. The maximum and minimum were 3821 and 2 µg/m³, respectively.

2.4 Environmental Fate

There are no environmental fate data available for *n*-heptane.

3.0 Toxicology of *n*-Heptane

The following toxicological review of *n*-heptane is primarily focused on the inhalation data since this route of exposure is the predominant path of human exposure and *n*-heptane is primarily released into the environment in the vapour phase. Data on other exposure media are included where relevant or where inhalation data is lacking.

It has been suggested that *n*-heptane is absorbed readily through respiration. Due to the lipophilic nature of *n*-heptane, absorbed *n*-heptane is largely distributed to the fat, followed by the brain, muscle, liver, kidney, heart, lung and blood. In rats, two of the major metabolites of *n*-heptane identified in the urine were 2-heptanol and 3-heptanol, which were eliminated as sulphates and glucuronide conjugates. A small amount of 2,5-heptanedione (0.13%) was also found in the urine. Since the formation of 2,5-heptanedione is metabolically unfavourable and this γ -diketone metabolic product is a very minor metabolite of *n*-heptane, it has been suggested that the neurotoxic effects of *n*-heptane are much less significant than those of *n*-hexane (Low *et al.*, 1987).

3.1 Acute Toxicity

The primary health concern associated with *n*-heptane intoxication is its narcotic and depressant effect on the central nervous system (Low *et al.*, 1987). Short-term exposures of volunteers to *n*-heptane at 1000 ppm (4090 mg/m³) for 6 min., or 2000 ppm (8180 mg/m³) for 4 min., showed slight vertigo. Exposure to 5000 ppm (20450 mg/m³) for 4 min., resulted in marked vertigo, inability to walk a straight line and incoordination. Exposure to the same concentration for 15 min. induced hilarity or a state of stupor for at least 30 min. in some volunteers and there were complaints of slight nausea, loss of appetite, lassitude, and a gasoline-like taste that lasted for several hours after exposure.

Inhalation exposure of mice to *n*-heptane at 10000 - 15000 ppm (40900 - 61350 mg/m³) induced narcosis within 30 - 60 min. Exposure to 9800 ppm (40080 mg/m³) for 2 hours resulted in prostration. Prostration and loss of reflexes occurred prior to convulsion and death in mice exposed to *n*-heptane at 13000 - 19000 ppm (53170 - 77710 mg/m³) within 15 - 40 min. Deep anaesthesia developed in mice exposed to 32000 ppm (130880 mg/m³) of *n*-heptane for 5 min., and at 48000 ppm (196320 mg/m³), 75% of the animals developed respiratory arrest within 4 min. (Low *et al.*, 1987). In a few animal studies, respiratory irritation, breathing irregularities and respiratory arrest have been observed in mice exposed to high concentrations, those at or above 32000 ppm or 130880 mg/m³, of *n*-heptane (Low *et al.*, 1987).

3.2 Subchronic and Chronic Toxicity

There is no clear information in *n*-heptane-induced neurotoxicity in workers or in chronic exposures in humans. Cases of neuropathy were reported in workers exposed to aliphatic solvent mixtures containing pentane, hexane and heptane. Some workers showed clinical signs of anorexia, aesthenia, paraesthesia, fatigue, and bilateral symmetrical muscle paralysis mostly found in the legs. Electrophysiological studies indicated that there were diffuse and symmetrical peripheral nerve changes. It was suggested that the observed polyneuropathy (a disease process involving peripheral nerves, e.g. distal or sensory motor nerves) was attributable to the neurotoxic effect of hexane (Low *et al.*, 1987; ACGIH, 1991; WHO, 1991).

Rats of both sexes exposed to 400 - 3000 ppm (1630 - 12270 mg/m³) *n*-heptane for 6 hours/day, 5 days/week for 26 weeks did not show signs of neurological abnormalities or organ/tissue toxicity (e.g. to the haematopoietic system). An increase in the levels of serum alkaline phosphatase in the female rats exposed to 3000 ppm (12270 mg/m³) was noted, but blood chemistry studies indicated no renal, hepatic or haematological abnormalities. In another study, rats exposed to 1500 ppm (6135 mg/m³) *n*-heptane for 9 hours/day, 5 days/week for 30 weeks, did not develop noticeable neurotoxicity. Similarly, no neurobehavioural changes or neuropathy were observed in rats exposed to *n*-heptane at 3000 ppm (12270 mg/m³) for 12 hours/day, 7 days/week for 16 weeks (Low *et al.*, 1987).

3.3 Developmental/Reproductive Toxicity

No information was identified.

3.4 Genotoxicity and Carcinogenicity

In a few genotoxicity studies with *n*-heptane, results were negative. These studies include: several strains of *Salmonella typhimurium* and two strains of *Escherichia coli* with or without metabolic activation (reverse mutations); *Saccharomyces cerevisiae* with or without metabolic activation (gene conversion); and a rat liver epithelial cell line (chromosome aberration test) (U.S. EPA, 1998). The US EPA indicated that there was no human or animal data available to assess the carcinogenicity of *n*-heptane (US EPA, 1998).

3.5 Environmental Effects

No information was identified.

4.0 Existing Ambient Air Quality Criteria

4.1 Overview

No Ambient Air Quality Criterion or standard for *n*-heptane has been established for Ontario (MOEE, 1994a).

The documentation of ten agencies including, the United States federal government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal government, was reviewed for the existence and basis of air quality criteria for *n*-heptane. Agency-specific summaries of information concerning air quality guidelines for *n*-heptane are presented in Section 11.0, in the Appendix of this report. A brief summary is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria, based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

The Commonwealth of Massachusetts has developed criteria for alkanes/alkenes in general. Of these, *n*-hexane may not exceed 25% by proportion (MDEP, 1995).

Michigan state has derived an 8-hour Initial Threshold Screening Level (ITSL) of $3500 \mu\text{g}/\text{m}^3$ based on the REL-TWA (recommended exposure level, time-weight-average) of $350 \text{ mg}/\text{m}^3$ (85 ppm) from NIOSH, the National Institute for Occupational Safety and Health (NIOSH, 1988).

The New York State guideline is based on the extrapolation from the occupational limit of $350 \text{ mg}/\text{m}^3$ (85 ppm) of NIOSH. The short-term guideline concentration is $83000 \mu\text{g}/\text{m}^3$ and the annual guideline concentration is $830 \mu\text{g}/\text{m}^3$.

Table 1. Summary of Existing Air Quality Guidelines¹ for *n*-Heptane

Agency	Guideline Value ²	Basis of Guideline	Date ³	Comments
U.S. EPA (IRIS)	no ambient air exposure limits are available			
California	no ambient air exposure limits are available			
Massachusetts	TEL (Threshold Effects Exposure Limits): none for <i>n</i> -heptane only; 95.24 µg/m ³ (24-hour average) for alkanes/alkenes.	REL-TWA from NIOSH.	1995	Adjusted to allow for exposures via other media; not to exceed 25% <i>n</i> -hexane by proportion.
Michigan	3500 µg/m ³ (8-hour average)	TLV-TWA from NIOSH	1998	
New Jersey	no ambient air exposure limits are available			
New York	83000 µg/m ³ (1-hour average) 830 µg/m ³ (annual average)	TLV-TWA from NIOSH	1990	Used for permitting
Netherlands	no ambient air exposure limits are available			
WHO	no ambient air exposure limits are available			
Sweden	no ambient air exposure limits are available			
CEPA	no ambient air exposure limits are available			
Ontario	no ambient air exposure limits are available			

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Using conditions of 1 atmosphere and 10°C, 1.0 µg/m³ = 0.274 ppb. Various agencies use conversion factors based on a range of temperatures, varying between 0°C to 25°C. Depending on the selected temperature, conversion of units may vary slightly.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

4.2 Evaluation of Existing Criteria

Available toxicological information suggests that the predominant toxicological effects of *n*-heptane are narcotic and depressant effects (ACGIH, 1991; NIOSH, 1977). The acute toxicity of *n*-heptane in humans is similar to that of *n*-hexane for their depressant effects on the central nervous system, e.g. vertigo, giddiness. However, *n*-heptane (at 4090 mg/m³ and 8180 mg/m³ for 6 and 4 min., respectively) appears to be slightly more toxic in inducing vertigo than *n*-hexane (no effect at about 7000 mg/m³ for 10 min.; effective at about 17000 mg/m³). Similarly, prostration and loss of reflexes followed by convulsion and death occurred, in mice exposed to *n*-heptane at 13000 - 19000 ppm (53170 - 77710 mg/m³) within 15 - 40 min., whereas comparable effects occurred in mice exposed to *n*-hexane at 38000 ppm (133760 mg/m³). The difference in the narcotic responses may be explained by the notion that the alkane concentrations required to induce a physiologic response decrease as the number of carbon atoms in the compound increases (NIOSH, 1977).

There is no information to assess the health effects of chronic exposure to *n*-heptane in humans. Based on limited data from animal studies, it is suggested that *n*-heptane is of low toxicity. For example, no neurotoxic effects were observed in rats treated continuously with *n*-heptane at 3000 ppm or 12270 mg/m³ for up to 30 weeks. On the other hand, chronic exposure to *n*-hexane induced polyneuropathy in humans and animals (WHO, 1991). Neurotoxic effects, such as lesions in the peripheral nerve and decreased conduction velocity in sensory/motor nerves in humans, and lesions in both of the peripheral and central nervous systems and decreased nerve conduction velocity in animals, of *n*-hexane have been described as unique to this compound and some other hexacarbon solvents, such as methylbutyl ketone (ACGIH, 1991; WHO, 1993). These discrepancies in neuropathy effects may be attributed to the differences in the metabolism of these substances and, the toxic effects of their respective metabolites. One of the major metabolites of *n*-hexane, 2,5-hexanedione, has been suggested as the neuropathologic agent of this hexacarbon solvent (WHO 1991). On the other hand, the structurally similar γ -diketone metabolite of *n*-heptane, 2,5-heptanedione, is only *quantitatively* a very minor metabolic by-product of this heptacarbon solvent, and, as of yet, no information is available to suggest that 2,5-heptanedione is toxicologically active in humans or animals.

Studies on the carcinogenic and reproductive/teratogenic effects of *n*-heptane have not been reported, and it was suggested that this compound may not have these effects (NIOSH, 1977; Low *et al.*, 1987). Genotoxicity test results from a few studies reviewed were negative (U.S. EPA, 1998).

Of the agency guidelines studied, only three state agencies, the states of Massachusetts, Michigan and New York, have developed air quality criteria for *n*-heptane. The Massachusetts criteria, derived for alkanes/alkenes as a group, are based on the REL-TWA (recommended exposure level, time-weight-average) of the NIOSH (NIOSH, 1988). The REL-TWA of 350 mg/m³ for alkane/alkene compounds includes petroleum distillates, *n*-pentane, *n*-octane, and Stoddard Solvent. For the purpose of the air

guidelines, the Massachusetts Department of Environmental Protection (MDEP) assumed a mixture of equal parts of *n*-pentane, *n*-hexane, *n*-heptane and *n*-octane and stipulates that *n*-hexane cannot exceed 25% in proportion, likely to avoid the neurotoxic effect of this alkane (MDEP, 1990; MDEP, 1994).

Michigan state has derived their 8-hour Initial Threshold Screening Level (ITSL) of $3500 \mu\text{g}/\text{m}^3$ based on the REL-TWA of $350 \text{ mg}/\text{m}^3$ (85 ppm) from the NIOSH, by applying an uncertainty factor of 100.

The State of New York considers *n*-heptane to be of moderate toxicity. The New York State guideline is also based on an extrapolation from the occupational limit of NIOSH ($350 \text{ mg}/\text{m}^3$ or 85 ppm). The NIOSH REL-TWA was divided by 4.2 to convert from the occupational exposure to a continuous environmental exposure, to arrive at New York's short-term guideline concentration (SGC) of $83000 \mu\text{g}/\text{m}^3$. The REL-TWA was divided by 420 to obtain the annual guideline concentration (AGC).

One common observation is that all three agencies adopted the REL-TWA of $350 \text{ mg}/\text{m}^3$ of NIOSH as the sole basis for their guideline development, and no detailed scientific assessment for *n*-heptane has been performed. The major difference appears to lie in the application of uncertainty factors to extrapolate from this occupational limit to their environmental criteria. The uncertainty factor of 3675 used by the state of Massachusetts can be considered overly conservative, particularly including the factor of 5 (or 20%) to account for relative source contribution, i.e. from air (see Appendix 9.3 for derivation). Considering the volatile nature of this solvent, exposures from sources other than air are most likely of minor relevance. The uncertainty factor of 100 used by the agency of Michigan to derive its air guideline is a default value. New York state converted the exposure time of a 40-hour work week to a continuous exposure in order to derive its short-term guideline concentration (1-hour), based on the REL-TWA of NIOSH. Thus, a factor of 4.2 was applied. A further uncertainty factor of 100 was applied to the SGC to derive the annual guideline concentration for New York.

The rationale supporting the NIOSH guideline needs to be examined. The NIOSH occupational limit of $350 \text{ mg}/\text{m}^3$ was established to offer a sufficient margin of safety to protect against the development of chronic nerve disorders in workers exposed to aliphatic solvent mixtures ($\text{C}_5 - \text{C}_8$) (NIOSH, 1977 & 1988). On a volume/volume basis, this value is equal to about 85 ppm of *n*-heptane and 100 ppm for *n*-hexane. The $350 \text{ mg}/\text{m}^3$ was recommended based on the observation that workers developed polyneuropathy after chronic exposures to *n*-hexane or mixtures of industrial solvents containing *n*-hexane, *n*-heptane, *n*-pentane, *n*-octane and/or cycloalkanes. This neurotoxic effect was observed at *n*-hexane concentrations below 500 ppm ($1800 \text{ mg}/\text{m}^3$). From animal studies in mice, a *n*-hexane concentration of 100 ppm ($360 \text{ mg}/\text{m}^3$) did not induce clear neurotoxic effects. Based on these human and animal studies, a guideline concentration of $350 \text{ mg}/\text{m}^3$ was determined for alkanes ($\text{C}_5 - \text{C}_8$) as the workplace environmental limits.

Both the ACGIH and OSHA agreed that the *n*-hexane-induced polyneuropathy should be considered in the development of their respective occupational guidelines, and recognized that industrial or technical grade *n*-heptane solvents often contain some *n*-hexane. Originally, the ACGIH derived its occupational limit of 500 ppm (2045 mg/m³) for *n*-heptane based on the acute central nervous system effect (dizziness) of this heptacarbon solvent. Later, the ACGIH revised its limit to 400 ppm (1640 mg/m³) to account for the concern of polyneuropathy because of the possible existence of *n*-hexane in mixtures of hydrocarbons in numerous cases, despite that there was no clear evidence that *n*-heptane may induce polyneuropathy (NIOSH, 1977). The OSHA agrees with the ACGIH but supports the earlier ACGIH occupational limit of 500 ppm (2045 mg/m³) for its PEL-TWA (permissible exposure level, time-weighted-average). Countries such as Germany and Finland appear to be in agreement with the OSHA and have established occupational limits of 500 ppm (2045 mg/m³), while the U.K. and Australia recognized 400 ppm (1640 mg/m³) as the maximum allowable concentration for the workplace (cited in ACGIH, 1991 and NIOSH, 1977). Ontario (the Ministry of Labour) has established an occupational exposure limit of 400 ppm (TWA-EV, time-weighted-average).

5.0 Responses of Stakeholders to the Information Draft

In January, 1999, the Ministry posted information draft documents for eighteen chemicals, including *n*-heptane, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and any technical or economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received one submission from a stakeholder regarding the draft document for *n*-heptane. A stakeholder from the automotive coatings industry suggested that the occupational exposure limit derived by ACGIH is the most appropriate basis for setting a standard for *n*-heptane.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for heptane. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In some cases, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for *n*-Heptane

Available toxicological information indicates that the predominant adverse effects of *n*-heptane are narcotic and depressant effects, which may occur at exposure concentrations around 1000 ppm (4090 mg/m³). There is no clear evidence to indicate that chronic exposure to this chemical, at concentrations above the occupational limits of 400 ppm (1640 mg/m³) or 500 ppm (2045 mg/m³), could induce significant health effects or physiological changes in humans or animals. It is unlikely that chronic exposure to *n*-heptane alone could induce polyneuropathy, which has been considered unique to *n*-hexane exposure.

Only three U.S. state agencies have promulgated air quality guidelines. All three were derived from the occupational limit of the NIOSH. The differences in the values of these air quality guidelines reside essentially in the application of uncertainty and/or modification factors to provide sufficient margin of safety in the extrapolation of these occupational limits to environmental criteria. Air quality criteria derived from the NIOSH occupational limit may result in an overly conservative consideration of the adverse health concerns of *n*-heptane. The NIOSH limit was developed using *n*-hexane as the surrogate toxicant for short chain alkanes. This approach may not be valid since the polyneuropathological effect of *n*-hexane appears to be unique to this hexacarbon solvent and is not exhibited by other short chain alkanes.

The occupational limit of the ACGIH can be considered a reasonable alternative. The ACGIH considered the predominant narcotic and depressant effects of *n*-heptane and also recognized the possible concomitant existence of some *n*-hexane (for its neurotoxic effect) in the commonly used industrial grade *n*-heptane.

Since no sufficient human or animal data is available to provide a reliable dose-response relationship for a detailed risk assessment for *n*-heptane, using the occupational limits developed by the NIOSH or the

ACGIH will be reasonable alternatives. Of these, the toxicological considerations taken by the ACGIH are considered, scientifically, more relevant than those of the NIOSH.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the occupational exposure limit of 400 ppm (1640 mg/m³; TLV-TWA), established by the ACGIH of the U.S. The 8-hour TLV-TWA of 1640 mg/m³ is divided by a factor of 1.5 to convert from an 8-hour work day exposure to a 24-hour equivalent averaging time (MOE, 1987). The Ministry considers that the application of an uncertainty factor of 100 appropriate to avoid the adverse health effects of *n*-heptane in environmental exposures. Applying the uncertainty and exposure-time conversion factors to the TLV-TWA result in a 24-hour AAQC of 11,000 µg/m³.

The Ministry of the Environment uses a factor of 3 to derive POIs from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion and half-hour Point Of Impingement standard for *n*-heptane:

- a 24-hour average AAQC of 11,000 µg/m³ (micrograms per cubic metre of air) for *n*-heptane based on the adverse health effects of this compound; and,
- a half-hour POI standard of 33,000 µg/m³ (micrograms per cubic metre of air) for *n*-heptane based on the adverse health effects of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

-
- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;
 - MOE Guideline F-14 (formerly 02-01), "*Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects*" Economic Services Branch- April 1994 and;
 - "*Framework for the Application of Socio-economic Analyses in Setting Environmental Standards.*" Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for *n*-heptane can be sent to:

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Director, Standards Development Branch
Ontario Ministry of the Environment
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Toronto, Ontario
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**Fax: 416 327-2936
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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* *n*-Heptane (heptane)

2. *Agency:* U.S. Environmental Protection Agency

3. *Guideline Value(s):*
None

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities; however, values derived and presented in IRIS do not represent guidelines or standards, in and of themselves. IRIS also contains a summary of current American government regulatory actions under various legislative mandates.

5. *Documentation Available:*

U.S. EPA, 1995. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

Key Reference(s):

U.S. EPA, 1989. Health and Environmental Effects Document for *n*-heptane. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, as cited in U.S. EPA, 1998.

6. *Peer Review Process and Public Consultation:*

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature, were employed in the development of these values. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, within both the U.S. EPA and other science-based U.S. regulatory agencies. Information in IRIS is put forward for use after the results of the public review and comments on draft documents/information have been addressed.

7. *Status of Guideline:*

No guideline exists and no toxicity values to be used in risk estimation have been developed.

8. *Key Risk Assessment Considerations:*

The U.S. EPA considers *n*-heptane to be not classifiable as to human carcinogenicity because no human data and no animal data are available.

9. *Key Risk Management Considerations:*

None, since no guideline for ambient air exists.

10. *Multimedia Considerations of Guidelines:*

None are reported

11. *Other Relevant Factors:*

According to the U.S. EPA (1995), Brooks *et al.* (1988) reported that *n*-heptane gave negative results in several genotoxicity assays. No increases in reverse mutations were observed in *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100, and *Escherichia coli* strains WP2 and WP2 uvr A exposed to *n*-heptane at concentrations of up to 250 µg/mL in a pre-incubation assay. Assays were performed with and without rat-liver S9 preparations. *n*-heptane (up to 5 mg/mL) did not induce gene conversion in *Saccharomyces cerevisiae* JD1, in either the presence or the absence of rat-liver S9 preparation. No increase was observed in chromosome aberrations in the rat-liver epithelial cell line RL4 when exposed to *n*-heptane at concentrations up to 10 µg/mL.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* n-Heptane (heptane)

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

None

4. *Application:*

None

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

Key Reference(s):

None

6. *Peer Review Process and Public Consultation:*

None

7. *Status of Guideline:*

No current guideline

8. *Key Risk Assessment Considerations:*

None available

9. *Key Risk Management Considerations:*

None

10. *Multimedia Considerations of Guidelines:*

None

11. *Other Relevant Factors:*

None

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* *n*-Heptane (heptane) (CAS# 142-82-5)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

No Threshold Effects Exposure Limit (TEL) exists for *n*-heptane. However, a TEL exists for "Alkanes/Alkenes" mixtures, of which *n*-heptane may be a constituent and is not to exceed 25% by proportion. The TEL for Alkanes/Alkenes is $95.24 \mu\text{g}/\text{m}^3$ (24-hour average) and is based on consideration of threshold effects. No Allowable Ambient Limit (AAL) exists for *n*-heptane. However, an AAL exists for Alkanes/Alkenes mixtures, of which *n*-heptane may not exceed 25% by proportion. The AAL for Alkanes/Alkenes is $47.62 \mu\text{g}/\text{m}^3$ (annual average) and is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

Clement Associates, 1989. Structural Activity Relationships of Alkanes and Alkenes. A report prepared for Air Toxics Hotline. Clement Associates, Inc., Fairfax, Virginia. March 1989.

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

MDEP, (undated). Toxicity scoring worksheets for alkanes to develop the TEL and AAL for the Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. Peer-Review Process and Public Consultation:

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies and programs were reviewed: United States Environmental Protection Agency (U.S. EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

No guideline exists for *n*-hexane. The guideline for Alkanes/Alkenes is current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the U.S. EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of *n*-hexane, an IRIS RfC exists. However, the MDEP adopted an approach for assessing alkanes and alkenes as a group of chemicals sharing generally the same properties, including the mode of toxic action. Therefore, instead of using the IRIS RfC, the occupational limit was used. The Most Appropriate Occupational Limit (MAOL) was based on the NIOSH Recommended Exposure Limit (REL) of 350 mg/m³, which is generally applied to

alkane/alkene compounds including Petroleum Distillates (CAS # 8002-05-9), *n*-pentane (CAS # 109-66-0), *n*-octane (CAS # 111-65-9) and Stoddard Solvent (CAS # 8052-41-3). MDEP identified that these chemicals, as a group, tend to have irritant and narcotic effects and potentially some liver effects. For the purpose of the air guidelines, the MDEP assumed a mixture of equal parts *n*-pentane, *n*-hexane, *n*-heptane and *n*-octane. The MAOL of 350 mg/m³ was adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week, to consider continuous exposure.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 10 to account for the lack of low-level, chronic studies in both animals and humans.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, 735. The adjusted MAOL is numerically equivalent to 0.4762 mg/m³ (476.2 µg/m³). At this point, another set of uncertainty factors were applied to the adjusted MAOL:

- I. divided by 1. The Threshold Effects Uncertainty Factor (TEUF) is an uncertainty factor which accounts for acute, chronic, developmental or reproductive effects that may not have been considered in the health risk assessment of the occupational limit. The MDEP applied a score of 1 for *n*-heptane.
- II. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to the NIOSH REL is 3675. The TEL was, therefore, calculated as 95.24 µg/m³.

Non-Threshold Effects

MDEP has not identified alkane/alkene compounds' carcinogenic or mutagenic potential. The agency has identified that certain conjugated alkenes may have positive scores for structure-activity relationships, and therefore an uncertainty factor of 10 was applied in the derivation of the non-threshold exposure limit (NTEL). Using the adjusted MAOL of 476.2 µg/m³ as the starting point, a Non-threshold Effects Uncertainty Factor (NTEUF) of 10 was applied. The NTEL was calculated for Alkane/Alkene compounds as 47.62 µg/m³.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the NTEL for Alkane/Alkene compounds of 47.62 µg/m³ was adopted as the AAL.

9. *Key Risk Management Considerations:*

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. *Multimedia Considerations of Guidelines:*

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. *Other Relevant Factors:*

The TEL and AAL described above is applicable to *n*-heptane exposure if *n*-heptane does not exceed 25% of the mixture of alkanes.

MDEP chose not to develop a specific TEL and AAL for *n*-heptane in consideration of the NIOSH (1977) analysis that "...in most workplace situations, workers will be exposed to a mixture of alkanes rather than to a single alkane isomer. Because similar effects result from acute exposures to *n*-heptane and *n*-hexane and adverse effects produced by alkanes tend to increase as the carbon number of the alkane increases, it seems likely that components of an alkane mixture may exert additive toxic effects."

The MDEP reviews its recommended air guideline from time to time, and, in the future, may change the guideline for Alkanes/Alkenes to reflect the existence of the IRIS RfC for *n*-heptane. However, no such review is scheduled for the immediate future (MDEP, 1997).

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* n-Heptane (heptane) (CAS # 142-82-5)
2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)
3. *Guideline Value(s):* Initial Threshold Screening Level (ITSL) of 3500 $\mu\text{g}/\text{m}^3$, averaged over 8 hours.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL. As in the case of guidelines derived from the NIOSH REL-TWA which are legal limits of the U.S. Occupational Safety and Health Administration (OSHA). The NIOSH recommendations had been published in a variety of documents for reviews.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for *n*-heptane was adopted from the occupational exposure limit, REL-TWA, of 350 mg/m³ developed by the NIOSH, with the application of an uncertainty factor of 100. The ITSL is averaged over 8 hours.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* *n*-Heptane (heptane) (CAS # 142-82-5)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey does not have an air quality standard for *n*-heptane.

4. *Application:*

The Bureau of Air Quality Evaluation (BAQEv) Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

Key Reference(s):

None

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

None

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

None

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State

1. *Name of Chemical:* *n*-Heptane (heptane) (CAS# 142-82-5)

2. *Agency:* New York State

3. *Guideline Value(s):*

The recommended 1-hour average is 83,000 $\mu\text{g}/\text{m}^3$. The recommended annual average is 830 $\mu\text{g}/\text{m}^3$.

4. *Application:*

"... they are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212 and 257." (NYDEC, 1991, pg. 1). These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. Rather than being employed as legally enforceable, ambient air quality standards, the guidelines are to be employed to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

NYDEC, 1991. New York State Air Guideline -1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Albany, N.Y. 20 p. + Appendices.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. *Peer Review Process and Public Consultation:*

The scientific documents prepared by New York State employed peer-reviewed data and models, as well as the professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guideline development process, but specific information on the process for *n*-heptane was not presented in the available documentation.

7. *Status of Guideline:*

Current

8. *Key Risk Assessment Considerations:*

NYDEC (1991) has classified the toxicity of *n*-heptane as moderate. Compounds given the designation of moderate are animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans. For compounds in this classification, the short-term guideline was developed by dividing a chosen occupational standard by 4.2. The long-term guideline was developed by dividing a chosen occupational standard by 420. In the case of *n*-heptane, New York used the occupational standard, REL-TWA, of 85 ppm (350 mg/m³) (NIOSH, 1988).

9. *Key Risk Management Considerations:*

A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses as employed in the permitting process. The latest version of Appendix B of the New York State Air Guide -1 is dated April 4, 1994.

10. *Multimedia Considerations of Guidelines:*

Considers human airborne exposure only

11. *Other Relevant Factors:*

No information

11.7 Agency-Specific Summary: World Health Organization

1. *Name of Chemical:* n-Heptane (heptane) (CAS# 142-82-5)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

None

4. *Application:*

None.

5. *Documentation Available:*

World Health Organization (WHO), 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark. 426 p.

Key Reference(s):

None available

6. *Peer Review Process and Public Consultation:*

None

7. *Status of Guideline:*

No information

8. *Key Risk Assessment Considerations:*

None available

9. *Key Risk Management Considerations:*

None available

10. *Multimedia Considerations of Guidelines:*

None available

11. *Other Relevant Factors:*

None available

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* n-Heptane (heptane) (CAS# 142-82-5)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

None

4. *Application:*

None

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A review of environmental quality objectives and their policy framework in The. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment, The Hague, The Netherlands. 465 p.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulations Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

6. *Peer Review Process and Public Consultation:*

None

7. *Status of Guideline:*

No current guideline

8. *Key Risk Assessment Considerations:*

None available

9. *Key Risk Management Considerations:*

None

10. *Multimedia Considerations of Guidelines:*

None

11. *Other Relevant Factors:*

The Netherlands has set a target value for soil and sediment for *n*-heptane that is the chemical detection limit. The Chemical Waste Act concentration limit for aliphatic alkanes such as *n*-heptane is $\geq 50,000$ mg/kg.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* n-Heptane (heptane) (CAS# 142-82-5)
2. *Agency:* According to Dr. K. Victorin of the Swedish Institute of Environmental Medicine (pers. comm.), no official Swedish air quality guidelines have been promulgated by the Swedish Environmental Protection Agency.
3. *Guideline Value(s):*
None
4. *Application:*
None
5. *Documentation Available:*
Victorin, K., 1993. Health effects of urban air pollutants: guideline values and conditions in Sweden. Chemosphere, 27:1691-1706.
6. Peer Review Process or Public Consultation:
None
7. *Status of Guideline:*
No current guideline
8. *Key Risk Assessment Considerations:*
n-Heptane is neurotoxic at high concentrations but has not been evaluated (Victorin, 1993).
9. *Key Risk Management Considerations:*
No information
10. *Multimedia Considerations of Guidelines:*
No information
11. *Other Relevant Factors:*
No information

11.10 Agency Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* *n*-Heptane (heptane) (CAS # 142-82-5)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. *n*-Heptane is not included in the Priority Substances Lists (PSL1 and PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (+PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects. Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

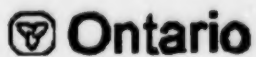
MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either ' <i>Reference Exposure Level</i> ' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or ' <i>Recommended Exposure Limit</i> ' used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₉₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
n-HEXANE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. *n*-Hexane was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1976. A review of scientific and technical information relevant to setting an ambient air quality standard for *n*-hexane has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for *n*-hexane.

n-Hexane (CAS # 110-54-3) is a clear, colourless, highly volatile liquid. It has a faint odour and an odour threshold of 458 mg/m³. *n*-Hexane is used in various industrial processes as a solvent such as in vegetable oil extraction, coatings, paints, rubber polymerization, and adhesives. *n*-Hexane is also used in low-temperature thermometers, and in the manufacturing of pharmaceuticals and other products.

n-Hexane is absorbed rapidly through the lungs after inhalation and is distributed throughout the body. Most of the absorbed *n*-hexane is subsequently excreted, unchanged, in exhaled air, although some is excreted as metabolites in both exhaled air and urine. Symptoms of exposure to *n*-hexane include sensorimotor polyneuropathy, cranial neuropathy, visual disturbances, dizziness, headaches, and fatigue. In animals, the peripheral and central nervous systems, and the male reproductive system are affected by *n*-hexane exposure. The neuropathological effect of *n*-hexane may be potentiated by methyl ethyl ketone. There are limited data on the carcinogenic potential of *n*-hexane.

Environment Canada has monitored ambient air levels for *n*-hexane from January 1993 to December 1995 from thirty-nine monitoring stations across Canada. From 4,233 samples nation-wide a mean concentration of $2.03 \pm 2.87 \mu\text{g}/\text{m}^3$ was obtained, with sampled concentrations ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $35.26 \mu\text{g}/\text{m}^3$. In Ontario, a range of 0.02 to a maximum of $110 \mu\text{g}/\text{m}^3$ of *n*-hexane was detected from 1994 to 1996. The highest concentrations monitored were in the vicinity of Sarnia in 1994 ($110 \mu\text{g}/\text{m}^3$), and an asphalt plant in Vineland in 1996 ($95 \mu\text{g}/\text{m}^3$).

Ontario currently has an AAQC for *n*-hexane. The half-hour POI guideline is $35,000 \mu\text{g}/\text{m}^3$ and the 24-hour AAQC is set at $12,000 \mu\text{g}/\text{m}^3$. These criteria have been established on the basis of health effects.

In revising the air quality standards for Ontario, the Ministry of the Environment is considering risk assessments, and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, and the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Of these, the US EPA, the states of Michigan, New Jersey, New York and California have developed (or are proposing to develop) criteria for *n*-hexane. The Commonwealth of Massachusetts, has developed criteria for alkanes/alkenes in general, of which *n*-hexane may be a constituent (not to exceed 25% by proportion). The US EPA has developed a Reference Concentration (RfC) of 200 $\mu\text{g}/\text{m}^3$ for *n*-hexane. This RfC is based on an epidemiological study of neurotoxic effects (functional impairment of the peripheral nervous system in several test items) in humans for occupational settings.

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and accepted the scientific studies which support the development of the Reference Concentration (RfC) established by the United States Environmental Protection Agency (US EPA). After reviewing additional toxicological information, the Ministry considers the uncertainty factors used to derive the RfC of 200 $\mu\text{g}/\text{m}^3$ by the US EPA reasonable and thus a 24-hour AAQC of 200 $\mu\text{g}/\text{m}^3$ is proposed for Ontario.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for *n*-hexane:

- **a 24-hour average Ambient Air Quality Criterion (AAQC) of 200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) based on the adverse health effects of this compound and the possible interaction with other hydrocarbon solvents.**

Based on supporting science and dispersion modelling, a half-hour POI standard of 600 $\mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of 35,000 $\mu\text{g}/\text{m}^3$ to this revised level of 600 $\mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim Point Of Impingement standard from the following range of values:

- **600 $\mu\text{g}/\text{m}^3$ to 6000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for *n*-hexane, based on the adverse health effects of this compound and the possible interaction with other hydrocarbon solvents.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

n-Hexane was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information published subsequent to the development of the existing standards in 1976. A review of scientific and technical information relevant to setting an ambient air quality standard for *n*-hexane had been provided in a previous document for stakeholder comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour point of impingement (POI) standard for *n*-hexane.

2.0 General Information

2.1 Physical and Chemical Properties

The following list provides some general information on *n*-hexane and its properties:

CAS #	110-54-3
RTECS #	MN9275000
UN #	1208
Conversion Factors	1 ppm = 3.52 mg/m ³ @ 25 °C and 760 mm Hg 1 mg/m ³ = 0.284 ppm @ 25 °C and 760 mm Hg
Boiling Point	69 °C
Flash Point	-21.7 °C
Henry's Law Constant	Range of 50,586 - 190,000 Pa m ³ /mol
Log K _{OW}	3.9
Formula	C ₆ H ₁₄
Molecular Weight	86.2 g/mol
Vapour Density (air = 1)	2.97
Vapour Pressure	150 mm @ 25 °C
Common Synonyms	<i>n</i> -hexane, hexyl hydride, Skellysolve B

n-Hexane is a clear, colourless, highly volatile liquid with a faint odour (Lewis, 1991; WHO, 1991). An odour threshold for *n*-hexane has been reported to be 458 mg/m³ (ACGIH, 1991). It is poorly soluble in water and soluble in most organic solvents, including ethanol and ether (ACGIH, 1991; WHO, 1991). Purified *n*-hexane consists of 95-99.5% *n*-hexane with small amounts of other *n*-hexane isomer impurities (WHO, 1991). Commercial-grade hexane consists of a mixture of *n*-hexane isomers as well as cyclopentane, cyclohexane, pentane, and heptane (ACGIH, 1991; WHO, 1991). Hexane may comprise from 20-80% of commercial *n*-hexane (ACGIH, 1991; WHO, 1991).

2.2 Uses of *n*-Hexane

Commercial hexane is used in various industrial processes, including, as a solvent in vegetable oil extraction, coatings, paints, rubber polymerization, and adhesives (ACGIH, 1991; WHO, 1991). *n*-Hexane is also used as a laboratory chemical, in low-temperature thermometers, and in the manufacture of pharmaceuticals and other products (WHO, 1991).

2.3 Sources and Levels

n-Hexane occurs naturally in natural gas and crude oil. It is also produced industrially. *n*-Hexane is not listed in Environment Canada's National Pollutant Release Inventory for environmental release reporting by the industries (NPRI, 1997).

Environment Canada has ambient air data for *n*-hexane levels from January 1993 to December 1995 from thirty-nine monitoring stations across Canada. From 4,233 samples, a mean concentration of $2.03 \pm 2.87 \mu\text{g}/\text{m}^3$ was observed. The reported concentrations ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $35.26 \mu\text{g}/\text{m}^3$ (Environment Canada, 1997).

In Ontario between 1994 to 1996, unscheduled monitoring results indicate that the half-hour average concentrations for *n*-hexane varied from $0.02 \mu\text{g}/\text{m}^3$ (the detection limit) to a maximum of $110 \mu\text{g}/\text{m}^3$. The highest concentrations monitored were in the vicinity of Sarnia in 1994 ($110 \mu\text{g}/\text{m}^3$) and in Vineland in 1996 ($95 \mu\text{g}/\text{m}^3$) (MOEE, 1997). In two separate special monitoring surveys performed in 1997, the average and maximum half-hour concentrations down-wind from a facility at Sarnia were 9 and $64 \mu\text{g}/\text{m}^3$, respectively. At another site in the Greater Toronto Area, the average and maximum half-hour concentrations down-wind from a facility were 5 and $19 \mu\text{g}/\text{m}^3$, respectively (MOE, 1998b). Recent monitoring data provided by the Lambton Industrial Society, indicated that a general down trend was observed in the annual average concentrations for *n*-hexane from 1994 to 1998 in Sarnia (6.9 to $3.4 \mu\text{g}/\text{m}^3$) and Corunna (4.3 to $1.8 \mu\text{g}/\text{m}^3$) (LIS, 1999). No consistent pattern for the maxima was observed; the maxima values ranged from $49.2 \mu\text{g}/\text{m}^3$ in 1995 to $8.4 \mu\text{g}/\text{m}^3$ in 1997 in Sarnia and from 24.1 in 1994 to 7.8 in 1997 in Corunna. The maximum hourly averages in Sarnia between 1995 and 1996 were 154 to $380 \mu\text{g}/\text{m}^3$ (detection limit was $0.64 \mu\text{g}/\text{m}^3$) (LIS, 1997).

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 32 facilities with emissions of *n*-hexane covered by a Certificate was identified. These approvals were for emissions from a variety of industries in pharmaceuticals, food packaging, automotive products, plastic and metal products, petroleum products and chemical products. The median Ground Level Concentration (GLC) estimated by Regulation 346 dispersion modelling for all 32 sources was approximately $32 \mu\text{g}/\text{m}^3$. The maximum and minimum were 3601 and $0.024 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

Most transport of *n*-hexane occurs in the vapour phase after emission into the environment since its water solubility is very low ($9.5 \text{ mg}/\text{L}$ at 25°C). *n*-Hexane is not expected to affect the physical properties of the atmosphere, to deplete the ozone layer, or to alter precipitation patterns. The rate constant for the reaction of hydroxyl radicals with *n*-hexane ranges from 5.63×10^{-12} to $6.2 \times 10^{-12} \text{ cm}^3/\text{sec}$ (WHO, 1991). Based on degradation by hydroxyl radicals alone, the half-life of *n*-hexane in

the troposphere is estimated to be 2 to 2.4 days (WHO, 1991). Similar hydrocarbons undergo the conversion to form smog, but *n*-hexane is one of the least photochemically reactive hydrocarbons (WHO, 1991)

3.0 Toxicology of *n*-Hexane

The following toxicological review of *n*-hexane is primarily focussed on the inhalation route of exposure since this is the predominant route of human exposure. Data on other exposure media are included where relevant or where inhalation data is lacking.

n-Hexane is absorbed rapidly through the lungs after inhalation exposure and is distributed throughout the body. Most of the absorbed *n*-hexane is metabolized to a number of substances which have been identified in the urine of workers exposed to *n*-hexane, including 2,5-hexanedione (considered to be the neurotoxic agent), 2,5-dimethylfuran, γ -valerolactone, and some 2-hexanol (WHO, 1991; ATSDR, 1997). Approximately 10-20% of *n*-hexane absorbed through inhalation is excreted unchanged in the exhaled air. In rats, 2-hexanol was the major metabolite identified in the urine during urine collection and accounted for about 60 - 70% of total metabolites collected (WHO, 1991; ATSDR, 1997). The main target organ of *n*-hexane is the nervous system.

3.1 Acute Toxicity

Effects of acute exposure to *n*-hexane in humans include irritation to the eyes, nose, and throat, blurred vision, and neurotoxicity at relatively high concentrations. Inhalation of *n*-hexane at 7,040 mg/m³ for 10 minutes did not induce any neurobehavioural symptoms, whereas exposure to 17,600 mg/m³ for 10 minutes resulted in vertigo and giddiness (ACGIH, 1991; WHO, 1991). Drowsiness was observed as a result of exposure to *n*-hexane concentrations of 3,520 to 89,760 mg/m³ for 30-60 minutes (WHO, 1991). Volunteers exposed to *n*-hexane vapour at 1,760 mg/m³ for 3-5 minutes did not experience eye irritation (WHO, 1991).

n-Hexane has low toxicity to animals in acute exposures. A 1-hour inhalation LC₅₀ of 271,040 mg/m³ (77,000 ppm) has been observed in male Fischer rats (WHO, 1991). Mice exposed to *n*-hexane at concentrations above 133,760 mg/m³ (38,000 ppm) showed loss of postural reflexes followed by death. Ataxia and decreased motor activity were noted in Sprague-Dawley rats following exposures to *n*-hexane at concentrations between 302,720 to 316,800 mg/m³ (86,000 - 90,000 ppm) for 25 to 30 minutes. Rats exposed to 84,480 mg/m³ (24,000 ppm) *n*-hexane for 10 minutes did not show any behavioural effects. Histopathological changes of the lung tissues (lamellar inclusions in type II pneumocytes) were noticed in Wistar rats exposed to *n*-hexane at 35,200 mg/m³ (10,000 ppm) for 4 or 8 hours or to 24,640 mg/m³ (7,000 ppm) for 8 hours; there were no effects in intrapulmonary

nerves. *n*-Hexane appears to be toxic to the male reproductive system. Testicular lesions, degeneration of the primary spermatocytes and mild exfoliation of spermatids, were observed in Sprague Dawley rats exposed to 17,600 mg/m³ (5000 ppm) for 24 hours. Rats recovered completely 30 days after the cessation of treatment.

3.2 Subchronic and Chronic Toxicity

Case studies of occupational exposure to *n*-hexane show that exposure for intermediate (15 to 365 days) and long (over one year) periods of time results in peripheral neuropathy (degeneration of nerve endings) in humans (ATSDR, 1997). The ATSDR has established a minimum risk level for chronic inhalation exposure of 0.6 ppm or 2,100 µg/m³. This was derived from a study of workers exposed to approximately 58 ppm (210,000 µg/m³) for an average of 6 years.

The most frequently observed adverse effects of long-term exposure to *n*-hexane in humans are sensorimotor polyneuropathy, cranial neuropathy, blurred vision, and abnormal colour vision (as reviewed in US EPA, 1998, in ATSDR, 1997 and in WHO, 1991). Symmetrical paraesthesia and weakness are the first few signs of *n*-hexane neuropathy, with the lower extremities usually affected first. Also accompanying neuropathy is a marked reduction in conduction velocity in sensory and motor nerves. Nerve biopsy showed axonal lesions of the large myelinated fibres with axonal swellings followed by myelin retraction at the node of Ranvier. There was only a mild to moderate reduction in the number of fibres, mainly of large myelinated fibres. The small myelinated or unmyelinated fibres were seldom affected. Muscle biopsy indicated signs of myofibrillar atrophy. Recovery from neuropathy is gradual and slow and residual neuropathy may persist for a few years. Headache, anorexia, and dizziness, muscular weakness, blurred vision, and fatigue may precede or coincide with the neuropathy. Clinical examination indicated that reduced body weight and decreased or absent reflexes were noticeable (WHO, 1991). Neuropathy has been reported to occur at exposure concentrations ranging from 97 to 8,125 mg/m³ (30 to 2500 ppm), and overt neuropathy may be observed only after two months to five years of exposure (WHO, 1991). Cases of polyneuropathy have been reported in workplaces where *n*-hexane was used as; a mixing solvent in tungsten carbide milling, as a glue solvent in vinyl sandal making, as a machine cleansing agent in press proofing, or with other solvents in shoe manufacturing (WHO, 1991; ATSDR, 1997).

Sanagi *et al.* (1980, as cited in WHO, 1991; US EPA, 1998 & ATSDR, 1997), carried out an epidemiological study on two age-matched groups of workers at a tungsten carbide alloy factory to investigate the neurotoxicity of *n*-hexane. *n*-Hexane was used in the production of tungsten carbide alloys. Fourteen workers under 50 years of age, who worked in ball milling and drying of tungsten carbide alloy operations, were studied. The exposure durations ranged from 1 to 12 (mean: 6.2) years. The control group used consisted of 14 workers from the sintering workshop, who were not exposed to *n*-hexane. The mean concentration of *n*-hexane, for the 8-hour time-weighted-average

exposure period over a 2-years, was 204 mg/m³ (58 ppm). The average concentrations for acetone in the workplace ranged from 52 - 164 mg/m³ (22 - 69 ppm). Clinical and electro-physiological examinations were performed in this study.

In the exposed group, headache, hyperaesthesia (abnormal acuteness of sensation of touch or pain) in the limbs and muscle weakness were reported most often. Paraesthesia (abnormal sensation of burning, tickling or tingling) was reported in three exposed workers and one control worker. A slightly higher prevalence of diminished bicipital and patellar tendon reflexes was observed in the exposed group. Significant effects on muscle strength (jump test on one foot) and vibration sensation (tuning fork) were noted in the exposed group. There were no abnormalities identified in the cranial nerves, the pyramidal tract or peripheral motor nerves. Electro-physiological examination did not reveal any neuropathy in any worker, but in the exposed group, the mean maximal motor conduction velocities in the posterior tibial nerve were significantly reduced as compared with those in the control group. Moreover, the mean distal latency of the posterior tibial nerve was significantly increased in the exposed group. These observations were consistent with the *n*-hexane-induced peripheral neuropathy observed in animals. The US EPA identified a LOAEL of 58 ppm (204 mg/m³) for neurological effects in this study (Sanagi *et al.*, 1980). This LOAEL was based on an 8-hour time-weighted-average for occupational exposure and was adjusted to a value of 73 mg/m³ for continuous exposure in the general population.

Similar neuropathological effects of *n*-hexane were also observed in animals (as reviewed in WHO, 1991 and ATSDR, 1997). The sequence of events in neuropathy in rats has been detailed. The first sign of neuropathy appears to begin with an increase in the number of 10 nm axonal filaments, and the accumulation of swellings on the proximal side of the nodes of Ranvier in the distal regions of large myelinated fibres. With continuous exposures, a retrograde spread of axonal swellings up the nerve occur, and smaller myelinated and unmyelinated fibres may become involved. The nerve terminal is unaffected until later in the process. The enlarged axons displace the paranodal myelin sheaths leaving denuded swellings in areas near the nodes of Ranvier. This process occurs before functional impairment is evident and can be reversed on cessation of exposure. When exposure ceases, swelling diminishes and proliferation of Schwann cells occurs at these sites with subsequent remyelination of the axons. With continuous exposure to *n*-hexane, axonal restoration and remyelination do not occur at all swellings, and the section of the nerve fibre between the swelling and the terminal undergoes breakdown. However, axonal spouting is often seen at the intact portion of a degenerated fibre even while intoxication continues. This regenerative process can re-establish motor and sensory function when intoxication ends.

The nerve fibres most vulnerable to *n*-hexane in rats were branches of the nerves innervating the muscles of the hind limbs (in the sequence of order: tibial nerves for the calf muscles, plantar nerves for the flexor digitorum brevis muscle and the sensory plantar nerves for the digits). When exposure

continues, axonal degeneration may ascend the plantar and tibial nerves. The most sensitive fibres appear to be the largest. It has been demonstrated that *n*-hexane, or its toxic metabolite, 2,5-hexanedione, can induce axonal swelling and degeneration in the central nervous system including the areas such as the medulla oblongata and the spinal cord.

Sprague-Dawley rats were exposed to *n*-hexane between 1408 - 2112 mg/m³ (400 - 600 ppm) for 1 to 23 weeks. Axonal swellings were observed in the hind limb nerves (tibial and plantar nerves) and in the central nervous system (medulla oblongata and the spinal cord and the cerebellar vermis) and these occurred before the weakness of the hind limbs was noticed. Male CD rats were exposed to *n*-hexane at 440 or 1760 mg/m³ (125 or 500 ppm) for 22 hours/day, 7 days/week. Axonal swelling was noticed in the tibial nerve and the medulla oblongata after 2 months of exposure to 1760 mg/m³. After 6 months of exposure, pronounced degeneration and loss of axons in the tibial and sciatic nerves, the lumbar spinal cord and the medulla oblongata was observed. Recovery of these neuropathological effects noted at 1760 mg/m³ (500 ppm) was complete by 6 weeks after the cessation of the treatment. Male Fischer-344 rats exposed to 3520 mg/m³ (1000 ppm) *n*-hexane for 24 hours/day, 5 days/week for 11 weeks developed inhibition of spontaneous motor activity. Hind limb grip strength was diminished and the fore limb grip strength was less affected. Multi-sensory conditioned avoidance response and pole-climbing ability decreased after 8 weeks, but recovered between weeks 18 and 36. In two separate studies, exposure of rats to *n*-hexane at 440 mg/m³ (125 ppm) for about 22 hours/day, 7 days/week for 26 to 34 week, did not induce observable clinical or histological peripheral or central neurotoxicity.

Tail nerve conduction velocity was reduced in male Wistar rats exposed to *n*-hexane at 3696 mg/m³ (1050 ppm) for 12 hours/day, 7 days/week for 16 weeks. There was no definite clinical signs of neurotoxicity. Clinical signs of neurotoxicity were noticed when rats were exposed to 10560 mg/m³ (3000 ppm). No significant effects on tail nerve conduction time in rats were observed following exposure to *n*-hexane at 373 mg/m³ (106 ppm) for 12 hours/day, 7 days/week for 24 weeks; histological examination of one rat indicated that the tail nerve was normal. However, when rats were exposed to *n*-hexane at 722 or 1725 mg/m³ (205 or 490 ppm) for 24 weeks, axonal swellings and demyelination were evident in the tail nerves at the concentration of 722 mg/m³. A higher no-observed-effect-level was obtained from male Wistar rats exposed to *n*-hexane at 1795 mg/m³ (510 ppm), using daily 8-hours exposures for 33 weeks; no effects on tail nerve structure or function were noted.

Sprague-Dawley rats of both sexes exposed to *n*-hexane up to 35200 mg/m³ (10000 ppm) for 6 hours/day, 5 days/week for 13 weeks did not show changes in neurological functions (posture, gait, tone and symmetry of the facial muscles, pupillary reflexes, palpebral reflexes, extensor thrust, cross-extensor thrust). Isolated and greatly enlarged axons were noted in the medulla of one male rat in the 35200 mg/m³ group; no other histopathological lesions were observed in the brain. Peripheral axonopathy of the tibial nerve was noticed in 4 of 5 male rats in the 35200 mg/m³ group and 1 male in

the 22880 mg/m³ (6500 ppm) group. The lesions were at an early stage of development and consisted of paranodal axonal swellings in nerve fibres. Segmental demyelination and axonal degeneration were not evident. No consistent changes were observed in any females or males from the 10560 mg/m³ (3000 ppm) group.

It was also found that exposure of male Wistar rats to *n*-hexane at 2464 mg/m³ (700 ppm) for 8 hours/day, 7 days/week for up to 40 week did not result in signs of clinical neurotoxicity. In contrast, male Wistar rats exposed to 1760 or 2464 mg/m³ (500 or 700 ppm) *n*-hexane for 22 hours/day, 7 days/week for 9 weeks showed signs of narcosis. Weakness in hind limbs of exposed animals developed, leading to paralysis, and eventually to quadriplegia. Complete hind limb paralysis was seen in the ninth week in the 1760 mg/m³ group. Rats exposed to 2464 mg/m³ developed hind limb paralysis in the fourth week of exposure. Histological examination indicated axonal swellings of the tibial nerve and portions of the ischiatic nerve. Breakdown of the axons and demyelination were observed distal to the swellings. Axonal swellings were also evident in the spinal cord near the cervical region. It would appear that the development of neuropathy may be related to whether exposures to *n*-hexane are intermittent (6 - 8 hours/day) or continuous (22 - 24 hours/day), however, this needs to be studied further.

In one study, B6C3F mice were exposed to *n*-hexane at 0, 1760, 3520, 14080 and 35200 mg/m³ (0, 500, 1000, 4000 and 10000 ppm) for 6 hours/day, 5 days/week for 13 weeks. In addition, mice were also exposed to 3520 mg/m³ for 22 hours/day, 5 days/week for 13 weeks. The only neurobehavioural effect observed was a decrease in locomotor activity in female mice exposed to 35200 mg/m³ for 6 hours/day. At this concentration, paranodal swellings were not noted in the control mice, but swellings of the tibial nerves were observed in 3 out of 4 male and 3 out of 4 female mice. In the treatment group of 3520 mg/m³ for 22 hours/day, similar paranodal swellings were observed. The severity of the lesion was mild and no segmental demyelination, distal axon degeneration or axonal swellings in the spinal cord were noted. This insensitivity could be related to the relatively short length and smaller diameter of the myelinated axon, as compared to rats or humans (Dunnick *et al.*, 1989 as cited in US EPA, 1998 & ATSDR, 1997). In addition to the effects on axonal swelling, *n*-hexane exposure at 1000 ppm (3520 mg/m³) also induced mild inflammatory, erosive and regenerative lesions in the olfactory and respiratory epithelia of the nasal cavity.

Inhaled *n*-hexane also induced other systemic effects such as mild inflammatory lesions of the nasal epithelium. In an animal study reported by Dunnick *et al.* (1989), subchronic inhalation of *n*-hexane was carried out by exposing male and female B6C3F₁ mice (10/sex/dose) to 0, 500, 1,000, 4,000, and 10,000 ppm (0, 1,762, 3,525, 14,099, and 35,247 mg/m³, respectively) for 6 hours per day, 5 days per week for 13 weeks (duration adjusted exposure calculated as 0, 315, 629, 2,518, and 6,294 mg/m³). An additional group of mice was exposed to 1,000 ppm (3,525 mg/m³) for 22 hours per day, 5 days per week for 13 weeks (duration adjusted exposure calculated as 2,308 mg/m³). Toxicity was

assessed by examining both behavioral and physiological (e.g. body weight, organ weight, organ tissues, etc.) endpoints of toxicity. Histopathological changes included mild inflammatory, erosive and regenerative lesions in the olfactory and respiratory epithelium of the nasal passages of the mice exposed to 2,308 mg/m³ and greater. Multifocal regeneration and metaplasia in the olfactory epithelium were observed at 3525 mg/m³. Minimal lesions were observed in the 315 and 629 mg/m³ groups. Other neurohistopathological evidence of toxicity was observed in 6 of the 8 animals in the 2,309 mg/m³ group and 6 of the 8 animals in the 6,294 mg/m³ dose group, but not in 8 of the 10 animals in the control group.

3.3 Developmental and Reproductive Toxicity

Developmental or reproductive studies on humans were not available. *n*-Hexane does not appear to cause embryotoxic or teratogenic effects. Pregnant albino rats were exposed to 3,489 mg/m³ *n*-hexane (99% pure) vapour for 6 hours/day during days 8 to 16 of gestation. Although significantly depressed postnatal growth was observed up to 3 weeks after birth, growth returned to normal by 7 weeks. No difference from controls was noted in fetal resorption, birth weight or other abnormalities (as reviewed in US EPA, 1998). *n*-Hexane vapour (99.9% purity) at concentrations of 0, 705, 3,525, or 17,623 mg/m³ was administered to pregnant rats for 20 hours/day for 14 consecutive days from days 6 to 19 of gestation (as reviewed in US EPA, 1998). Maternal toxicity was indicated by reduction in weight gain in all exposure groups, but was statistically significant only at the highest concentration. There was no significant difference in the incidence of fetal malformations or other reproductive indicators, such as the number of implantations, the mean percent of live pups per litter, the mean percent of resorptions per litter, or the fetal sex ratio compared to controls. *n*-Hexane caused testicular damage in adult male Sprague-Dawley rats exposed to 3,525 mg/m³ 18 hours/day for 61 straight days. A total loss of the germ cell line in a fraction of the animals was observed up to 14 months post-exposure (as reviewed in US EPA, 1998). In contrast, no treatment-related reproductive effects were observed in the seminal vesicles, prostate, testis and epididymis of male Sprague-Dawley rats exposed to *n*-hexane at 1760 mg/m³ (500 ppm) for 22 hours/day for 6 months (as reviewed in ATSDR, 1997). Similarly, no reproductive tissue lesions were noticed in male F-344 rats (in testis, seminal vesicles, prostate or epididymis) or in female rats (in ovaries, uterus, vagina, cervix) exposed to *n*-hexane at 10560, 22880 or 35200 mg/m³ (3000, 6500, or 10000 ppm) for 6 hours/day, 5 days/week for 13 weeks (as reviewed in WHO, 1991 & ATSDR, 1997).

3.4 Genotoxicity

The limited mutagenicity testing conducted on *n*-hexane indicates little potential for genotoxicity (ATSDR, 1997). An *in vitro* study in which Chinese hamster ovary cells were exposed to undiluted liquid *n*-hexane in the absence of a metabolizing fraction resulted in chromosomal damage (as reviewed in WHO, 1991). There was no significant increase in point mutations in cultured mammalian cells or

bacteria, nor DNA damage in bacteria as a result of *n*-hexane exposure (as reviewed in WHO, 1991). No increase in unscheduled DNA synthesis was found in human lymphocytes *in vitro*. Chromatid breaks in rat bone marrow cells were reported in an *in vivo* study (as reviewed in WHO, 1991). *n*-Hexane did not induce dominant lethal mutations (for germ cell mutation test) in male CD-1 mice treated with 99 ppm (350 mg/m³) or 396 ppm (1400 mg/m³) *n*-hexane for 6 hours/day, 5 days/week for 8 weeks (as reviewed in ATSDR, 1997).

3.5 Carcinogenicity

There are limited data on the carcinogenic potential of *n*-hexane. Dermally applied, *n*-hexane did not result in the enhanced formation of skin tumours in mice after exposure to 7,12-dimethylbenzanthracene, a tumour initiator, or following co-exposure with croton oil, a promoting agent (WHO, 1991). Papillary tumours have been reported in bronchiolar epithelium of rabbits after 24 week exposure to 3,000 ppm (11,000 mg/m³) (Lungarella *et al.*, 1984, as cited in ATSDR, 1997).

3.6 *n*-Hexane in Solvent Mixtures

Solvents in commercial applications, for example solvents in the glue used in the shoe manufacturing industry, often contain *n*-hexane and other solvents, such as methyl ethyl ketone (MEK), methylisobutyl ketone (MIBK) and toluene. There have been reports that some of these solvents may enhance the neurotoxic effect of *n*-hexane (ATSDR, 1997; WHO, 1991).

It has been suggested that MEK potentiates the neurotoxic effects of *n*-hexane. Two thousand cases of solvent abuse, which resulted severe polyneuropathy in Germany in 1974, led to research on the potential for MEK to enhance the adverse health effects of *n*-hexane, and on the interactions of MEK with other hexacarbon solvents (as reviewed in WHO, 1993 & ATSDR, 1997). Victims of solvent abuse often found development of paraesthesia and weakness in leg and arm muscles. Neurophysiological and histological findings indicated reduction in motor and sensory nerve conduction velocities and were in proportion to the degree of paresis. Damages to the nerves were also reported. The outbreak of neuropathy in solvent abuse victims coincided with the change of solvent formulation from one with *n*-hexane, benzene fraction, ethyl acetate and toluene to a similar solvent mixture with less (16%) *n*-hexane and the addition of 11% MEK. It was suggested that MEK potentiated the neuropathy of *n*-hexane.

Similar findings were obtained from animal studies. It has been demonstrated that the neurotoxicity of *n*-hexane is potentiated by methyl ethyl ketone (MEK) under continuous exposure conditions (as reviewed in US EPA, 1998 & ATSDR, 1997 and WHO, 1991). *n*-Hexane-induced hind limb paralysis and related neuropathy were manifested after 9 weeks in all 5 Wistar rats exposed continuously to *n*-hexane at 1,760 mg/m³ (500 ppm), 22 hours/day, 7 days/week. These clinical signs

were present 1 week earlier in animals exposed to mixtures of 1,056 mg/m³ (300 ppm) *n*-hexane with 590 mg/m³ (200 ppm) MEK and 1,408 mg/m³ (400 ppm) *n*-hexane with 295 mg/m³ (100 ppm) MEK. Exposure to 1,760 mg/m³ *n*-hexane and 590 mg/m³ MEK resulted in complete hind limb paralysis after 4 weeks. Rats exposed to *n*-hexane at 2464 mg/m³ (700 ppm) or 1760 mg/m³ *n*-hexane + 590 mg/m³ (200 ppm) MEK for 8 hours/day, 7 days/week for 40 weeks did not show clinical signs of neuropathy. It appears that MEK potentiated the neurotoxic effect of *n*-hexane (shortened onset of neuropathological effect of *n*-hexane) under continuous exposure conditions, but not under intermittent exposures.

Understanding the possible mode of action of hexacarbon solvents in inducing neuropathy may explain the likely mechanism of MEK in the potentiation of the neurotoxic effects of *n*-hexane. It has been postulated that *n*-hexane is oxidized by hepatic microsomal enzymes to 2,5-hexanedione, the proximate neurotoxicant. The 2,5-hexanedione formed may induce cross-linking of neurofilaments and this may result in the blocking of transport at the node of Ranvier. The accumulation of neurofilaments may induce swelling proximal to the nodes and may lead to axonal degeneration distal to the nodes. In animal studies it was found that if the concentrations or doses of *n*-hexane or 2,5-hexanedione were high enough and sustained for long enough periods of time, clinical signs of neural degeneration were evident and were made more severe, or the onset of neuropathy was often shortened by the co-exposure with MEK (WHO, 1991 & 1993). Although MEK potentiation of the neurotoxic effects of *n*-hexane has frequently been observed in rats *in vivo*¹, information on the mechanism of action for MEK has not been well described. There are some suggestions that MEK may have metabolic interactions with *n*-hexane (WHO, 1993). Simultaneous inhalation exposure of *n*-hexane and MEK resulted in lower levels of 2,5-hexanedione (a common metabolite of *n*-hexane) in urine of rats *in vivo* and initially lower, but later somewhat elevated, levels of 2,5-hexanedione in serum *in vivo*. However, the increased 2,5-hexanedione level alone cannot explain the potentiation of *n*-hexane neurotoxicity. It appears that MEK may be involved in the activation of some components in the metabolism of *n*-hexane. Pretreatment of rats with MEK prior to inhalation exposure to *n*-hexane resulted in higher levels of 2,5-hexanedione in several tissues, including blood (WHO, 1993). There are, as of yet, insufficient information to delineate the mechanism of MEK in enhanced hexacarbon solvent neurotoxicity. It may be of relevance to note that MEK has been demonstrated to potentiate the hepatotoxic effects of haloalkane solvents, such as carbon tetrachloride and chloroform, through a possible mechanism of increased bioactivation of haloalkanes.

¹ For more information on the MEK potentiated neurotoxic effects of hexacarbon solvents and haloalkanes in animals, see WHO, 1993.

3.7 Environmental Effects

There are a lack of data on the effects of *n*-hexane on terrestrial wildlife. Since *n*-hexane has low water solubility and is highly volatile, it is primarily found in air. The risk of exposure of aquatic organisms is likely to be low and transient except for uncontrolled discharges into surface waters. A few laboratory experiments have been conducted on the water flea, *Daphnia magna*, however these experiments were static tests and the actual *n*-hexane concentration was not measured during the course of the experiment, resulting in LC₅₀ values of >1,000 mg/L (Bringmann *et al*, 1982 as cited in WHO, 1991). Another experiment conducted on *Daphnia magna* in a closed, airtight container determined a 48-h LC₅₀ of 3.9 mg/L, but does not represent natural environmental conditions where *n*-hexane will rapidly volatilize from water (Bobra *et al*, 1983 as cited in WHO, 1991).

4.0 Existing Air Quality Criteria

4.1 Overview

Ontario currently has AAQCs for *n*-hexane. The half-hour POI guideline is 35,000 µg/m³ and the 24-hour AAQC is currently set at 12,000 µg/m³. These criteria have been established on the basis of health effects (MOEE, 1994a).

The documentation from ten agencies, including, the United States federal government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal government, was reviewed for the existence and basis of air quality criteria for *n*-hexane. A brief summary of this review is presented in Table 1, and agency-specific summaries of information concerning air quality guidelines for *n*-hexane are presented in Section 11.0. In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria, based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

None of the agencies reviewed considered *n*-hexane to be carcinogenic. Four agencies, the US EPA and the states of Michigan, New Jersey and New York, have developed reference values or criteria for *n*-hexane. The State of New York (for their Short-term Guideline Concentration, SGC, of 42,000 µg/m³) and the Commonwealth of Massachusetts (for their Threshold Effects Exposure Limit, TEL, of

47.62 $\mu\text{g}/\text{m}^3$) based their criteria on occupational exposure limits. The Commonwealth of Massachusetts has developed criteria for alkanes/alkenes in general, and assumed a mixture of equal parts *n*-pentane, *n*-hexane, *n*-heptane and *n*-octane; *n*-hexane as a constituent should not exceed 25% by proportion (MDEP, 1994).

The US EPA has developed a Reference Concentration (RfC) for *n*-hexane of 200 $\mu\text{g}/\text{m}^3$. This RfC is based on an epidemiological study by Sanagi et al. (1980) of neurotoxic effects (functional impairment of the peripheral nervous system in several test items) in humans in occupational settings. Michigan, New Jersey and New York adopted the RfC from the US EPA. The California Environmental Protection Agency has also recently proposed to adopt the RfC of the US EPA for its chronic inhalation REL (200 $\mu\text{g}/\text{m}^3$) (OEHHA, 1997). The Commonwealth of Massachusetts derived its annual average Allowable Ambient Limit (AAL) of 47.62 $\mu\text{g}/\text{m}^3$ for mixtures of alkanes and alkenes, based on occupational exposure limits.

Table 1. Summary of Existing Air Quality Guidelines^[1] for *n*-Hexane

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration): 200 µg/m ³ .	Epidemiological study of neurotoxic effects in humans.	1990	No air guideline promulgated.
California	Proposed chronic inhalation REL (Reference Exposure Level): 200 µg/m ³ .	RfC from US EPA	1997	<i>n</i> -hexane is identified on the June 1996 Toxic Air Contaminant Identification List
Massachusetts	TEL (Threshold Effects Exposure Limits): none for <i>n</i> -hexane only; 95.24 µg/m ³ (24-hour average) for alkanes/alkenes.	REL-TWA from NIOSH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): none for <i>n</i> -hexane only; 47.62 µg/m ³ (annual average) for alkanes/alkenes.	REL-TWA from NIOSH.	1995	Both the TEL and AAL are for Alkanes/Alkenes mixtures, of which <i>n</i> -hexane may not exceed 25% by proportion.
Michigan	ITSL (Initial Threshold Screening Level): 200 µg/m ³ (24-hour average).	RfC from US EPA.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC: 200 µg/m ³ (annual average)	RfC from US EPA.	1994	Permitting application. The RfC must be used in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): 42,000 µg/m ³ (1-hour average).	TLV-TWA from ACGIH.	1991	Used for permitting.
	AGC (Annual Guideline Concentration): 200 µg/m ³ .	RfC from US EPA.	1995	Used for permitting.
WHO	None.			
Netherlands	None.			
Sweden	None.			
CEPA	None.			
Ontario	half-hour POI guideline: 35,000 µg/m ³ .	Both the POI and AAQC are based on health.	1976	
	24-hour AAQC: 12,000 µg/m ³ .			

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.

4.2 Evaluation of Existing Criteria

The states of New York and Massachusetts base their short term criteria on occupational exposure limits. New York's Short-Term Guideline Concentration is based on the ACGIH TLV-TWA limit for *n*-hexane of 50 ppm (176 mg/m³) divided by 4.2 to extrapolate to continuous exposures. The Massachusetts 24 hour criterion, is derived for alkanes/alkenes as a group. They are based on the NIOSH REL-TWA for alkane/alkene compounds, including petroleum distillates, *n*-pentane, *n*-octane, and Stoddard Solvent, of 350 mg/m³ (NIOSH, 1988). For the purpose of air guidelines, the Massachusetts Department of Environmental Protection (MDEP) assumed a mixture of equal parts *n*-pentane, *n*-hexane, *n*-heptane and *n*-octane (MDEP, 1994).

The ACGIH and NIOSH have committees that review the human and animal toxicological responses for a substance, and make recommendations regarding the TLVs and RELs, respectively. The documentation available in support of these recommendations provides a summary of available toxicological data, particularly as it relates to occupational exposures. The method of extrapolation from the toxicological data to the TLV or REL is not clearly outlined and may incorporate a number of policy-related judgements.

The US EPA (1998) has calculated an RfC of 0.2 mg/m³ (200 µg/m³) for *n*-hexane. This RfC is based on an epidemiological study of neurotoxic effects (functional impairment of the peripheral nervous system in several test parameters) in humans in occupational settings. The US EPA (1998) cited two critical studies for establishing the RfC. They include; a human epidemiological study examining the neurotoxic effects of *n*-hexane (Sanagi *et al.*, 1980), and a mouse inhalation toxicity study for the adverse effect of *n*-hexane of the nasal cavity epithelium (Dunnick *et al.*, 1989²). The RfC for *n*-hexane was based on the human data derived from the study of Sanagi *et al.* (1980). The study of Dunnick *et al.* (1989) identified a NOAEL (no-observed-adverse-effect-level) and a lowest-observed-adverse-effect-level (LOAEL), both of which were based on mild inflammatory lesions of the nasal epithelium of mice³. The value of the LOAEL (human-equivalent-concentration) derived from this animal study, supports the LOAEL of the study of Sanagi *et al.* (1980), in which a NOAEL could not be derived. Furthermore, the data from the tungsten carbide alloy workers (Sanagi, *et al.*, 1980), provides considerable and compelling evidence that *n*-hexane is neurotoxic to humans.

² For a full discussion of the Dunnick *et al.* (1989) study, please refer to the Agency Specific Summary in Section 9.1, Federal Government of the United States.

³ Adverse effects (mild inflammatory lesions of the nasal epithelium) appear to have been identified at 315 mg/m³ (the reported NOAEL for this study). This raises questions concerning the identification of this dose level as a NOAEL, and, therefore, calls into question the identified LOAEL (629 mg/m³).

Sanagi et al. (1980) carried out an epidemiological study on two age-matched groups of workers of a tungsten carbide alloy factory. This study investigated the neurotoxicity of *n*-hexane. There were no neurological abnormalities observed. However, neurophysiological tests indicated that the exposed group exhibited significantly reduced mean motor nerve conduction velocities when compared to the control group. Other indices of neurological effects (e.g. slowed residual latency of motor nerve conduction) were significantly different in the exposed group when compared to the control group. These observations were consistent with the *n*-hexane-induced peripheral neuropathy observed in other studies in humans and animals (as reviewed in US EPA, 1998). The Sanagi et al. (1980) study identified the LOAEL for neurological effects as 58 ppm (204 mg/m³). This LOAEL was based on an eight-hour time weighted average for occupational exposure and was adjusted to a value of 73 mg/m³ for continuous exposure in the general population. The workers at this tungsten carbide alloy factory were also exposed to acetone concurrently with *n*-hexane. However, the effects of acetone exposure were not considered since there was an absence of evidence to suggest that acetone was toxic to the peripheral nervous system (Sanagi et al., 1980).

An uncertainty factor (UF) of 300 was applied to the adjusted LOAEL derived from the Sanagi et al. (1980) study. The factor of 300 is comprised of factors to, protect sensitive individual (UF=10), account for the use of a LOAEL rather than a NOAEL (UF=10), and an additional factor of 3 is to account for the lack of data on reproductive and chronic respiratory effects (US EPA, 1998). Therefore, the RfC is equal to the adjusted Sanagi et al. (1980) LOAEL of 73 mg/m³ divided by the uncertainty factor of 300, resulting in an RfC of 0.243 mg/m³, which the US EPA rounded down to 0.2 mg/m³. The US EPA (1998) gives an overall confidence rating of medium to the RfC. The key study is given a medium confidence since the LOAEL in this study (Sanagi et al., 1980) is based on neurotoxicity and this endpoint is supported by numerous other subchronic inhalation studies in animals and by human occupational studies. The database is given a medium confidence because there is a lack of appropriate reproductive studies and long-term inhalation studies.

The States of Michigan, New Jersey and New York (for its Annual Guideline Concentration) have promulgated air quality guidelines or reference concentrations for *n*-hexane by direct adoption of the US EPA's RfC. The California Environmental Protection Agency has recently proposed to adopt the RfC of the US EPA for its chronic inhalation REL (200 µg/m³) (OEHHA, 1997). This value is also based on the US EPA's RfC for the neurotoxic effect of *n*-hexane and alterations in the electrophysiology induced by this agent in humans (OEHHA, 1997).

The World Health Organization, the Netherlands, Sweden and the Canadian Federal government have not established air quality criteria for *n*-hexane.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including *n*-hexane, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards, and technical and economic impacts that may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received four submissions from various stakeholders regarding the draft document for *n*-hexane. Stakeholders in the automotive manufacturing industry suggested that the Ministry set a health-based AAQC of 600 $\mu\text{g}/\text{m}^3$ and a POI limit of 1,800 $\mu\text{g}/\text{m}^3$. It was also indicated that their facilities were operating at levels less than 1% of the current standard, recognizing however, that not all industries in Ontario can meet a proposed standard which was derived from the RfC of the US EPA and therefore a technical and economic analysis is needed. A stakeholder from the automobile equipment and parts industry suggested that the reference concentration derived from the ACGIH is the most appropriate and should be used to derive a standard. A stakeholder in the rubber industry noted that its current POI concentration is less than 10% of the current POI standard, but in two or three years its POI concentration will increase to about 10% of the current POI standard. A petroleum products stakeholder suggested that any significant decrease from the current standard would require a risk management analysis.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for *n*-hexane. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In

the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted, depending, on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for *n*-Hexane

Ontario currently has air quality standards for *n*-hexane. The half-hour POI guideline is 35,000 $\mu\text{g}/\text{m}^3$ and the 24-hour AAQC is set at 12,000 $\mu\text{g}/\text{m}^3$. These criteria were established on the basis of the health effects of this compound.

The most well documented toxic effect of *n*-hexane appears to be its toxicity in the peripheral nerves of humans. In animals, particularly rats, the peripheral and central nervous systems and the male reproductive system appear to be the major target organs. In either case, the metabolite 2,5-hexanedione has been suggested to be the toxic agent. Case studies of occupational exposure to *n*-hexane show that exposures for intermediate (15 to 365 days) and long (over one year) periods of time result in peripheral neuropathy (degeneration of nerve endings) in humans. The ATSDR has established a minimum risk level for chronic inhalation exposure of 0.6 ppm or 2,100 $\mu\text{g}/\text{m}^3$. This was derived from a study of workers exposed to approximately 58 ppm (210,000 $\mu\text{g}/\text{m}^3$) for an average of 6 years.

Available toxicological data does not suggest that *n*-hexane is a developmental toxicant, a teratogen, or a genotoxic agent. There are insufficient data to evaluate the carcinogenicity of *n*-hexane. It has been suggested that exposure to other common solvents, such as methyl ethyl ketone, methylisobutyl ketone and toluene, increases the toxicity of *n*-hexane. Since MEK is a common component of solvent mixtures in industrial uses, the effect of MEK may need consideration in *n*-hexane criteria development.

To derive its Reference Concentration (RfC), the US EPA used the adjusted LOAEL of 73,000 $\mu\text{g}/\text{m}^3$ obtained from the study of Sanagi *et al.* (1980). This agency applied an uncertainty factor of 300 to this LOAEL to obtain a RfC of 200 $\mu\text{g}/\text{m}^3$. Four U.S. State agencies have adopted this RfC for their air quality guidelines. The Ministry has considered the RfC an appropriate basis for the development of air quality standards for Ontario for the protection of health and the environment.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and accepted the scientific studies which support the development of the RfC established by the US EPA. After

reviewing additional toxicological information, the Ministry considers the uncertainty factors used by the US EPA to derive the RfC of 200 $\mu\text{g}/\text{m}^3$ reasonable and thus a 24-hour AAQC of 200 $\mu\text{g}/\text{m}^3$ is proposed for Ontario.

The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). On this basis, a POI value of 600 $\mu\text{g}/\text{m}^3$ can be obtained.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for *n*-hexane:

- a 24-hour average AAQC of 200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for *n*-hexane based on the adverse health effects of this compound and the possible interaction with other hydrocarbon solvents.

Based on supporting science and dispersion modelling, a half-hour POI standard of 600 $\mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current guideline of 35,000 $\mu\text{g}/\text{m}^3$ to this revised level of 600 $\mu\text{g}/\text{m}^3$, meeting this proposed POI standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- 600 $\mu\text{g}/\text{m}^3$ to 6000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for *n*-hexane, based on the adverse health effects of this compound and the possible interaction with other hydrocarbon solvents.

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

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- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;
 - MOE *Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
 - "*Framework for the Application of Socio-economic Analyses in Setting Environmental Standards.*" *Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.*
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for *n*-hexane can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS# 110-54-3)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The inhalation Reference Concentration (RfC) for *n*-hexane is 0.2 mg/m³ (200 µg/m³). No air concentration guidelines exist for *n*-hexane.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

Key Reference(s):

Dunnick, J.K., D.G. Graham, R.S. Yang, S.B. Haber and H.R. Brown, 1989. Thirteen-week toxicity study of *n*-hexane in B6C3F1 mice after inhalation exposure. *Toxicology*. 57(2):163-172.

Sanagi, S., Y. Seki, K. Sugimoto and M. Hirata, 1980. Peripheral nervous system functions of workers exposed to *n*-hexane at a low level. *Int. Arch. Occup. Environ. Health*. 47: 69-79.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

Current.

8. Key Risk Assessment Considerations:

The US EPA (1998) has calculated an RfC of 0.2 mg/m³ (200 µg/m³) for *n*-hexane. This RfC is based on an epidemiological study of neurotoxic effects (functional impairment of the peripheral nervous system in several test items) in humans in occupational settings. The US EPA chose two critical studies for establishing the RfC, i.e., Sanagi *et al.* (1980) and Dunnick *et al.* (1989). The primary reason described in IRIS for the selection of two critical studies was that a no-observed-adverse-effect-level (NOAEL) could not be derived from the Sanagi *et al.* (1980) study. The Dunnick *et al.* (1989) study identified a NOAEL and a lowest-observed-adverse-effect-level (LOAEL), both of which were based on mild inflammatory lesions of the nasal epithelium of mice⁴. The RfC for *n*-hexane was based on the human data derived from the Sanagi *et al.* (1980) study due to *n*-hexane's well documented human neurotoxic effects (US EPA, 1998).

Sanagi *et al.* (1980) carried out an epidemiological study on two age-matched groups of workers. This study investigated the neurotoxicity of *n*-hexane. Neurophysiological tests indicated that the exposed group exhibited significantly reduced mean motor nerve conduction velocities when compared to the control group. Other indices of neurophysiological effects (e.g. slowed residual latency of motor nerve conduction) were significantly different in the exposed group when compared to the control group. These observations were consistent with other studies in humans and animals (US EPA, 1998 and citations therein). The Sanagi *et al.* (1980) study identified the LOAEL for neurological effects as 58 ppm (204 mg/m³, assuming 25°C and 760 mm Hg). This LOAEL was based on an eight-hour time weighted average for occupational exposure. When converted to continuous exposure (assuming an occupational minute ventilatory volume of 10 m³/day and a daily minute ventilatory volume of 20 m³/day) the study LOAEL is adjusted as follows:

$$\begin{aligned}\text{Adjusted LOAEL} &= 204 \text{ mg/m}^3 \times (10 \text{ m}^3/\text{day} / 20 \text{ m}^3/\text{day}) \times (5 \text{ days}/7 \text{ days}) \\ &= 73 \text{ mg/m}^3 (73,000 \text{ µg/m}^3)\end{aligned}$$

The animal study by Dunnick *et al.* (1989) provided a LOAEL that was similar to the LOAEL identified in the Sanagi *et al.* (1980) study, and also identified a NOAEL. Both the NOAEL and LOAEL reported by Dunnick *et al.* (1989) are based on the effect observed as mild inflammatory lesions of the nasal epithelium of mice (portal-of-entry effects). In the Dunnick *et al.* (1989) study, subchronic inhalation of *n*-hexane was carried out using male and female B6C3F₁ mice (10/sex/dose) with dose groups as follows: 0, 500, 1,000, 4,000, and 10,000 ppm (0, 1,762, 3,525, 14,099, and 35,247 mg/m³, respectively). The exposure duration was six-hours per day, 5 days per week for 13

⁴Adverse effects (mild inflammatory lesions of the nasal epithelium) appear to have been identified at 315 mg/m³ (the reported NOAEL for this study). This raises questions concerning the identification of this dose level as a NOAEL, and, therefore, calls into question the identified LOAEL (629 mg/m³). The discussion of Dunnick *et al.* (1989) is included here because the US EPA has named it as one of the two critical studies for the *n*-hexane RfC.

weeks (duration adjusted exposure calculated as 0, 315, 629, 2,518, and 6,294 mg/m³). An additional group of mice was exposed to 1,000 ppm (3,525 mg/m³) for 22 hours per day, 5 days per week for 13 weeks (duration adjusted exposure calculated as 2,308 mg/m³). Toxicity was assessed by examining both behavioral and physiological (e.g. body weight, organ weight, organ tissues, etc.) endpoints of toxicity. Histopathological changes included mild inflammatory, erosive and regenerative lesions in the olfactory and respiratory epithelium of the nasal passages of the mice exposed to 2,308 mg/m³ and above. Multifocal regeneration and metaplasia in the olfactory epithelium were observed at 3525 mg/m³. Minimal lesions were observed in the 315 and 629 mg/m³ groups. Other neurohistopathological evidence of toxicity was observed in 6 of the 8 animals in the 2,309 mg/m³ group and 6 of the 8 animals in the 6,294 mg/m³ dose group, but not in 8 of the 10 animals in the control group. This study identified a NOAEL of 315 mg/m³ based on mild lesions. When adjusted for gas:respiratory effects (a factor of 0.122 derived by extrapolation of the surface area for respiratory tract and minute volume differences between humans and the test animal) the human equivalent NOAEL reported in IRIS is 38 mg/m³ (38,000 µg/m³) (US EPA, 1998). The next higher dose group was selected as the LOAEL and adjusted by the same procedure as used for the NOAEL. The human equivalent LOAEL is 629 mg/m³ x 0.122 = 77 mg/m³ (77,000 µg/m³). The human equivalent LOAEL derived from this study was similar to the LOAEL derived from the Sanagi *et al.* (1980) study (73 mg/m³).

The US EPA (1998) reported that the interpretation of the results from the Dunnick *et al.* study may be limited since neuropathological examinations were not carried out on all the tested dose groups. There were also discrepancies in the scoring system used in the paper to "grade" the presence of lesions. The average grade of the lesions in the LOAEL dose group was reported as "minimal to slight" and the average grade of lesions at the highest dose group ranged from "minimal to moderate". Other studies that examined *n*-hexane exposure did not exhibit a dose-response relationship in the severity or incidence of nasal lesions as presented in Dunnick *et al.* (1989).

An uncertainty factor (UF) of 300 was applied to the LOAEL derived from the Sanagi *et al.* (1980) study. The factor of 300 is comprised of factors to protect sensitive individuals (UF=10), the use of a LOAEL rather than a NOAEL (UF=10) and an additional factor of 3 to account for the lack of data on reproductive and chronic respiratory effects (US EPA, 1998).

Therefore, the RfC is equal to the adjusted LOAEL of 73 mg/m³ of Sanagi *et al.* (1980) divided by the uncertainty factor of 300, resulting in an RfC of 0.243 mg/m³ which the US EPA rounded down to 0.2 mg/m³. The US EPA (1998) gives a confidence rating of medium to the RfC and the data base, since the neurotoxicity endpoint identified in the epidemiological study of Sanagi *et al.* (1980) is supported by numerous other inhalation studies in animals and occupational studies from humans but there is a lack of reproductive and long-term inhalation studies.

The US EPA (1998) gives a confidence rating of medium to the RfC and the database.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No adjustment for multimedia exposure is considered in the development exposure concentrations for threshold effects or unit risk values for non-threshold effects.

11. *Other Relevant Factors:*

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS 110-54-3)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

No risk-based concentration limit has been established for *n*-hexane. Recently, the State of California has been proposing to adopt the RfC of 200 $\mu\text{g}/\text{m}^3$ from the US EPA for its chronic inhalation Reference Exposure Level for *n*-hexane.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. *Documentation Available:*

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 565-568.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, USA.

6. Peer-Review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification List is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS, etc.) and additional widely recognised reference texts.

The RfCs, Reference Exposure Levels (RELs) and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines is subject to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for *n*-hexane. The State understands and identifies that the US EPA has established a RfC of 200 $\mu\text{g}/\text{m}^3$ based on neurotoxicity and nasal epithelial lesions in humans (ARB, 1996). Though this is recognised by the State, *n*-hexane is not listed under Proposition 65 for the lack of activity as a reproductive or developmental toxicant, or as a carcinogen (ARB, 1996). Recently, The State of California has reconsidered the RfC of 200 $\mu\text{g}/\text{m}^3$ of the US EPA and proposed to adopt this value for its chronic inhalation Reference Exposure Level (OEHHA, 1997).

n-Hexane is listed on the June 1996 Toxic Air Contaminants Identification List (ARB, 1997) for further assessment.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). *n*-Hexane is not one of these substances.

11. *Other Relevant Factors:*

n-Hexane is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS# 110-54-3)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

No Threshold Effects Exposure Limit (TEL) exists for *n*-hexane. However, a TEL exists for "Alkanes/Alkenes" mixtures, of which *n*-hexane may be a constituent and is not to exceed 25% by proportion. The TEL for Alkanes/Alkenes is $95.24 \mu\text{g}/\text{m}^3$ (24-hour average) and is based on consideration of threshold effects. No Allowable Ambient Limit (AAL) exists for *n*-hexane. However, an AAL exists for Alkanes/Alkenes mixtures, of which *n*-hexane may not exceed 25% by proportion. The AAL for Alkanes/Alkenes is $47.62 \mu\text{g}/\text{m}^3$ (annual average) and is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

Clement Associates, 1989. Structural Activity Relationships of Alkanes and Alkenes. A report prepared for Air Toxics Hotline. Clement Associates, Inc., Fairfax, Virginia. March 1989.

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

MDEP, (undated). Toxicity scoring worksheets for alkanes to develop the TEL and AAL for the Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. US Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. Peer-Review Process and Public Consultation:

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies and programs were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

No guideline exists for *n*-hexane. The guideline for Alkanes/Alkenes is current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of *n*-hexane, an IRIS RfC exists. However, the MDEP adopted an approach for assessing alkanes and alkenes as a group of chemicals sharing generally the same properties, including the mode of toxic action. Therefore, instead of using the IRIS RfC, the occupational limit was used. The Most Appropriate Occupational Limit (MAOL) was based on the NIOSH Recommended Exposure Limit (REL) of 350 mg/m³, which is generally applied to alkane/alkene compounds including Petroleum Distillates (CAS # 8002-05-9), *n*-pentane (CAS # 109-66-0), *n*-octane (CAS # 111-65-9) and Stoddard Solvent (CAS

8052-41-3). MDEP identified that these chemicals, as a group, tend to have irritant and narcotic effects and potentially some liver effects. For the purpose of the air guidelines, the MDEP assumed a mixture of equal parts *n*-pentane, *n*-hexane, *n*-heptane and *n*-octane. The MAOL of 350 mg/m³ was adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week, to consider continuous exposure.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 10 to account for the lack of low-level, chronic studies in both animals and humans.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, 735. The adjusted MAOL is numerically equivalent to 0.4762 mg/m³ (476.2 µg/m³). At this point, another set of uncertainty factors were applied to the adjusted MAOL:

- I. divided by 1. The Threshold Effects Uncertainty Factor (TEUF) is an uncertainty factor which accounts for acute, chronic, developmental or reproductive effects that may not have been considered in the health risk assessment of the occupational limit. The MDEP applied a score of 1 for *n*-hexane.
- II. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to the NIOSH REL is 3675. The TEL was, therefore, calculated as 95.24 µg/m³.

Non-Threshold Effects

MDEP has not identified alkane/alkene compounds' carcinogenic or mutagenic potential. The agency has identified that certain conjugated alkenes may have positive scores for structure-activity relationships, and therefore an uncertainty factor of 10 was applied in the derivation of the non-threshold exposure limit (NTEL). Using the adjusted MAOL of 476.2 µg/m³ as the starting point, a Non-threshold Effects Uncertainty Factor (NTEUF) of 10 was applied. The NTEL was calculated for Alkane/Alkene compounds as 47.62 µg/m³.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the NTEL for Alkane/Alkene compounds of 47.62 µg/m³ was adopted as the AAL.

9. *Key Risk Management Considerations:*

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. *Multimedia Considerations of Guidelines:*

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. *Other Relevant Factors:*

The TEL and AAL described above is applicable to *n*-hexane exposure if *n*-hexane does not exceed 25% of the mixture of alkanes.

MDEP chose not to develop a specific TEL and AAL for *n*-hexane in consideration of the NIOSH (1977) analysis that "...in most workplace situations, workers will be exposed to a mixture of alkanes rather than to a single alkane isomer. Because similar effects result from acute exposures to *n*-hexane and heptane and adverse effects produced by alkanes tend to increase as the carbon number of the alkane increases, it seems likely that components of an alkane mixture may exert additive toxic effects."

The MDEP reviews its recommended air guideline from time to time, and, in the future, may change the guideline for Alkanes/Alkenes to reflect the existence of the IRIS RfC for *n*-hexane. However, no such review is scheduled for the immediate future (MDEP, 1997).

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* n-Hexane (hexane) (CAS # 110-54-3)
2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)
3. *Guideline Value(s):* Initial Threshold Screening Level (ITSL) of 200 $\mu\text{g}/\text{m}^3$, averaged over 24 hours.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1997. List of Screening Levels (ITSL, IRSL, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

Key Reference(s):

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL. Specifically, information from the US EPA's process for the development of reference concentrations (RfCs), upon which the ITSL for *n*-hexane is based, were employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for *n*-hexane was adopted from the RfC developed by the US EPA. The ITSL, which is averaged over 24 hours, equals the inhalation RfC (please refer to Section 5.1, Federal Government of the United States, for details regarding the derivation of the RfC).

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS # 110-54-3)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey does not have an air quality standard for *n*-hexane (NJDEP, 1997a). A reference concentration (RfC) of 200 $\mu\text{g}/\text{m}^3$ was adopted from the United States Environmental Protection Agency's (US EPA's) RfC which is based on neurotoxic effects in humans. This RfC is applied for the purposes of conducting risk assessments under the Air Quality Permitting Program.

4. *Application:*

The Bureau of Air Quality Evaluation (BAQEv) Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

Key Reference(s):

US EPA, 1998. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, D.C.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The US EPA's RfC, adopted by New Jersey as their RfC, should be used in risk assessments to estimate the public health risks for inhalation of *n*-hexane using the following equation:

$$\text{Hazard Quotient} = C / \text{RfC}$$

where: C = maximum annual average ambient air concentration in $\mu\text{g}/\text{m}^3$
 RfC = Inhalation RfC = $200 \mu\text{g}/\text{m}^3$

The RfC of $200 \mu\text{g}/\text{m}^3$ is adopted from the US EPA's Integrated Risk Information System (IRIS) (please refer to Section 5.1, Federal Government of the United States, for the derivation of the RfC). The maximum annual average ambient air concentrations of pollutants (C) are derived from one of three approaches: an initial risk screening assessment, dispersion modelling or air monitoring programs (NJDEP, 1997b).

Hazard quotients which are less than or equal to one indicate a risk which is considered to be negligible. However, hazard indices which are greater than one represent risks which are of concern to the State, and will be evaluated and managed on a case by case basis.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. For non-carcinogens, reference concentrations (RfCs) must be used for inhalation exposure, and reference doses (RfDs) for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS# 110-54-3)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

Short-term Guideline Concentration (SGC) for *n*-hexane is 42,000 µg/m³ (1-hour average) and the Annual Guideline Concentration (AGC) for *n*-hexane is 200 µg/m³.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

NYSDEC, 1997. Letter to Sylvia Miedinger, GlobalTox International Consultants Inc., dated February 5, 1997. Subject: Rationale Documents requested for New York State air quality standards. Author: Thomas Gentile, Chief, Toxic Assessment Section, Bureau of Stationary Sources, Division of Air Resources. New York State Department of Environmental Conservation. Albany, New York.

Key Reference(s):

ACGIH, 1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices 1990-1991. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. *Key Risk Assessment Considerations:*

n-Hexane is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC was derived from ACGIH Threshold Limit Value-Time Weighted Average (TLV-TWA) (1991) by dividing the ACGIH TLV-TWA (176 mg/m^3) by 4.2 and rounding up to 42 mg/m^3 ($42,000 \text{ } \mu\text{g/m}^3$). The US EPA's RfC of 0.2 mg/m^3 ($200 \text{ } \mu\text{g/m}^3$) for *n*-hexane was adopted as the AGC (please refer to Section 5.1, Federal Government of the United States, for details regarding the derivation of the RfC).

9. *Key Risk Management Considerations:*

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guideline considers only human exposure to contaminants in air.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS # 110-54-3)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

None.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*

Not applicable.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

9.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS # 110-54-3)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

n-Hexane is not classified under the Netherlands Emission Regulations. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long-term environmental quality objective which establishes a target value below which emissions of priority substances must be maintained. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological literature. This progressive approach will require facility-specific emissions to be kept below a limit or guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance or limit values are either air quality statutory requirements or non statutory regional-specific MIC levels.

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. *Peer-review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS# 110-54-3)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

Key Reference(s):

None available.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} .

No assessment has been carried out for *n*-hexane.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* *n*-Hexane (hexane) (CAS # 110-54-3)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

. *Guideline Value(s):*

No guideline has been established. *n*-Hexane is not included in the Priority Substances Lists (PSL1 and PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act*(CEPA). October, 1995.

6. *Peer-review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*
Not applicable.

11. *Other Relevant Factors:*
Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RFc	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RFd	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
HYDROGEN CHLORIDE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Hydrogen chloride (HCl) was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the establishment of the existing standard in 1988. A review of the scientific and technical information relevant to setting an ambient air quality standard for hydrogen chloride has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for hydrogen chloride.

Hydrogen chloride (HCl) is a colourless gas with a strong, pungent odour at ambient temperatures. It does not stay in the air in its gaseous form for very long. It is readily transformed into hydrochloric acid and washes down with precipitation. HCl is produced naturally in volcanoes and by chemical reactions in the atmosphere. However, the HCl that is measured in the atmosphere usually originates from man-made sources. HCl is used in a wide range of applications, such as a neutralising agent, ore refining, food processing, the manufacturing of fertilisers and dyes, as well as in the rubber and textile industries.

According to the 1997 National Pollutant Release Inventory (NPRI), 9,974 tonnes of hydrogen chloride were released to the atmosphere by 144 reporting facilities in Canada. In 1997, approximately 5,165 tonnes of HCl were reported to be released to the atmosphere in Ontario. This amounts to nearly 52 % of the national releases of 9,974. According to the NPRI, on a sectoral basis, approximately 85 % of Ontario's reported emissions to air came from the group of coal-fired electrical generating stations.

From 1992 to 1995, the Ministry of the Environment and Energy (MOEE) monitored ambient air concentrations of hydrogen chloride at four urban facilities (detection limit $\sim 1 \mu\text{g}/\text{m}^3$). Near a foundry where no proper air pollution control equipment was used, the concentration of HCl reached a maximum half-hour value of $490 \mu\text{g}/\text{m}^3$. In all cases where the appropriate air pollution control equipment was in operation, the observed ambient air concentrations were well below $100 \mu\text{g}/\text{m}^3$.

Hydrogen chloride is extremely corrosive and, as a result, the manufacturing, storage, and transportation processes are subject to rigorous safety standards. High concentrations of hydrogen chloride cause immediate irritation of the skin, eyes, and mucous membranes. Low levels of exposure cause mild irritation of the upper respiratory system (throat and nose) resulting in coughing and wheezing. During long-term exposure to moderate concentrations, erosion and discolouration of teeth has been reported. Daily exposure of workers to $7,500 \mu\text{g}/\text{m}^3$ of hydrogen chloride did not cause

noticeable adverse effects for the term of their working lives. The International Agency for Research on Cancer (IARC) and the US Environmental Protection Agency (EPA) have concluded that there is insufficient evidence to classify HCl as a potential carcinogen.

The current air quality standards for HCl in Ontario are $100 \mu\text{g}/\text{m}^3$ for the half-hour Point of Impingement standard and $40 \mu\text{g}/\text{m}^3$ for the 24-hour Ambient Air Quality Criterion (AAQC). These values are based on the corrosive effects of HCl.

In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the U.S. EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Of the criteria from these agencies reviewed, the Ministry has evaluated and accepted the scientific studies which support the development of the RfC by the US EPA. After reviewing additional toxicological information, the Ministry considers that it is reasonable to derive a 24-hour AAQC for HCl based on this RfC of $20 \mu\text{g}/\text{m}^3$. Based on dispersion modelling a calculated half-hour POI of $60 \mu\text{g}/\text{m}^3$ can be derived. In light of the corrosive nature of HCl, and comments from stakeholders, the Ministry has decided to maintain the current value of $100 \mu\text{g}/\text{m}^3$ as the POI standard. However, the Ministry has recommended a revised 24-hour AAQC of $40 \mu\text{g}/\text{m}^3$ for HCl. These air quality standards of HCl are considered to provide sufficient protection for human and environmental health as well.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and stakeholders' comments, the Ministry is proposing the following Ambient Air Quality Criterion and half-hour Point Of Impingement standard for hydrogen chloride:

- a 24-hour average AAQC of $20 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for hydrogen chloride based on the adverse health effects of this compound; and,
- a half-hour POI of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for hydrogen chloride based on the corrosive effect of this compound.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Hydrogen chloride was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the establishment of the existing standard in 1988. A review of scientific and technical information relevant to setting an ambient air quality standard for hydrogen chloride had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending an AAQC and a POI standard for hydrogen chloride.

2.0 General Information

2.1 Physical/chemical Properties

Hydrogen chloride (HCl) is a colourless gas at ambient temperatures. It has a strong and pungent odour and the fumes are choking and hygroscopic (absorbs moisture from the air). As a result of the variety of methods employed for measurement, there is no reliable odour threshold for hydrogen chloride. Reported odour thresholds vary from a low of 100 $\mu\text{g}/\text{m}^3$ to a high of 7,800 $\mu\text{g}/\text{m}^3$ (Cheminfo, 1996; WHO, 1982). Hydrogen chloride is recognized as having a corrosive effect on physical structures.

CAS #	2099047
RTECS #	MW4025000
UN #	1050 (anhydrous) 1789 (solution)
Conversion Factors	1 ppm = 1,500 $\mu\text{g}/\text{m}^3$ at 25°C
Boiling Point	-85°C
Henry's Law Constant	-
Flash Point	-
Water Solubility	Highly soluble 823 g/L at 32°F
Log K _{ow}	-
Formula	HCl
Molecular Weight	36.46
Vapour Density (air = 1)	1.268
Vapour Pressure	-
Common Synonyms	Hydrochloric acid

2.2 Uses of Hydrogen Chloride

Hydrogen chloride has wide applications, however it is mainly used as liquid hydrochloric acid. Hydrogen chloride is used as a pH adjusting agent, it is used in the manufacturing of alkyl chlorides, hydro-chlorination, polymerisation, alkylation and nitration reactions. It is also used in various industries such as the electronic, petroleum, steel pickling and other metal working, food processing, textiles and rubber manufacturing industries (Cheminfo, 1996; New Jersey, 1997).

2.3 Sources and Levels

Chlorides are ubiquitous in nature, and the burning of natural products will usually result in increases of hydrogen chloride in the ambient air (WHO, 1982). Volcanoes, along with chemical reactions in the atmosphere, are the principal natural sources of hydrogen chloride (HCl) but they contribute to only a very low natural background concentration (WHO, 1982). The gaseous state is the most likely form of HCl in the atmosphere, but because of its reactivity, it is rapidly neutralised or removed through reactions with other atmospheric constituents (Stevens *et al.*, 1992).

Man-made HCl is usually generated as a by-product of hydrocarbon chlorination processes and from dehydrohalogenation processes. It may be recycled in the process, diverted to an adjacent process, or purified and sold as liquid or anhydrous HCl. Some pure hydrogen chloride is made intentionally by reacting chloride with hydrogen, or sodium chloride and sulphuric acid. Since they contain chlorine, combustion of fossil fuels also produces hydrogen chloride. Hydrogen chloride emissions from coal-fired generating stations depends on the chlorine content of the coal, which can vary by a factor of ten or more. Combustion conditions and pollution control equipment can significantly affect the emissions to the atmosphere from coal combustion. Processes designed to control emissions of sulphur dioxide, such as limestone addition to the boiler and flue gas desulphurization, can be very effective in reducing emissions of HCl (Sloss, 1992).

According to the 1997 National Pollutant Release Inventory (NPRI), 9,974 tonnes of HCl were released to the atmosphere by 144 reporting facilities in Canada. Forty-six of these facilities were in Ontario and accounted for nearly 52 % (5,165 tonnes) of the total national emissions. According to the NPRI, on a sectoral basis, approximately 85% of Ontario's reported emissions to air came from coal-fired electricity generating stations.

Information on background concentration is limited. A sample of 95 recent applications for Certificates of Approval in Ontario were analysed. This analysis showed the median Ground Level Concentration estimated by Regulation 346 dispersion modelling to be $2.25 \mu\text{g}/\text{m}^3$, ranging from a low of 0.0005 and a high $138.6 \mu\text{g}/\text{m}^3$.

From 1992 to 1995, the MOEE monitored ambient air concentrations of hydrogen chloride at four urban facilities – two foundries, one municipal waste incinerator, and one hospital waste incinerator. The detection limit for hydrogen chloride was $1 \mu\text{g}/\text{m}^3$. Near the municipal waste incinerator the concentration never exceeded $5 \mu\text{g}/\text{m}^3$. Near the hospital biowaste incinerator, the concentration remained below $39 \mu\text{g}/\text{m}^3$. Near one foundry the concentration was always below $86 \mu\text{g}/\text{m}^3$. At another foundry, where no proper prevention equipment was used, the concentration varied between 1 and $490 \mu\text{g}/\text{m}^3$. When scrubbers were applied, these values ranged from less than 1 to a maximum of $62 \mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

Hydrogen chloride is predicted to exist primarily in a gaseous phase in the atmosphere. Under humid conditions, condensation can cause hydrogen chloride to become a component of acid fog. Hydrogen chloride, at very high concentrations, can be found in a particulate form in the atmosphere, but generally only for short periods of time. In the gas phase, hydrogen chloride is very reactive and is quickly neutralized or removed from the atmosphere via reactions with other substances. Due to high water solubility, hydrogen chloride can be transported over large distances in water as hydrochloric acid. Hydrogen chloride can contribute to the formation of acid precipitates; particularly in soils that have low buffering capacity and contain few nutrients (such as the Canadian Shield territory, corresponding to the northern part of Ontario).

3.0 Toxicology of Hydrogen Chloride

3.1 Acute Toxicity

At high concentrations, hydrogen chloride is highly corrosive to mucous membranes, and produces local irritations to the skin and the upper respiratory tract. The severity of these symptoms depends on the duration of exposure and the concentration in air. Exposure to 1,500,000 to 3,000,000 $\mu\text{g}/\text{m}^3$, even for short periods, causes a build-up of fluid in the lungs which can cause death. Its corrosiveness also applies to the eyes and skin. Exposure of the eyes to HCl causes immediate irritation, and greater exposure will lead to severe irritation and possibly burns as well as permanent blindness. Exposed skin or skin in contact with perspiration-soaked clothing might become irritated and burned in the prolonged presence of high concentrations of HCl (Cheminfo, 1996; WHO, 1982). Calabrese and Kenyon (1991) suggest that there is a possibility of adaptation to inhalation of hydrogen chloride. Concentrations of 15,000 $\mu\text{g}/\text{m}^3$, which are considered irritating at first, will become tolerable over time. After acclimation, exposures as high as 53,000 $\mu\text{g}/\text{m}^3$ can be tolerated (Cheminfo, 1996; Calabrese and Kenyon, 1991;). Stevens *et al.* (1992, as cited in US EPA, 1997), found no adverse respiratory effects of inhalation of low concentrations (1,200 $\mu\text{g}/\text{m}^3$ and 2,700 $\mu\text{g}/\text{m}^3$) and short exposure (45 minutes) of HCl in human subjects with mild asthma.

The one-hour LC_{50} of rats and mice were reported to be 4,700,000 $\mu\text{g}/\text{m}^3$ and 1,600,000 $\mu\text{g}/\text{m}^3$ respectively. In numerous animal studies, lethality was linked to respiratory injury such as pulmonary edema and emphysema (Calabrese and Kenyon, 1991). However, a study involving baboons, reported by the US EPA (1997) suggested that their more complex, upper airways removes more airborne chemical than other species. The baboons in this study were exposed to 15,000,000 $\mu\text{g}/\text{m}^3$ for five minutes, and did not show any abnormalities from three days to three months later. There is evidence that different species are affected differently by HCl. Baboons and humans are much less sensitive to

HCl than other mammalian species, especially mice. In another study (also reviewed in US EPA, 1997), 30-minute LC_{50} values were reported to be 7,100,000 $\mu\text{g}/\text{m}^3$ and 4,000,000 $\mu\text{g}/\text{m}^3$ for rats and mice, respectively. The LC_{50} values for five minute exposure were 61,000,000 $\mu\text{g}/\text{m}^3$ and 21,000,000 $\mu\text{g}/\text{m}^3$ for rats and mice, respectively. This study suggests that mice are two to three times more sensitive than rats to HCl exposure.

The extreme corrosiveness of hydrogen chloride to material, and the severe burns or irritations it can cause to humans, animals or plants, induces prompt repairs of any leak or spills in the production, transportation or usage processes. This generally results in limited worker exposure and almost non-existent exposure of the general population except in emergency conditions such as fires or major spills. Because HCl gas is very reactive, it rapidly associates with water and is transformed into hydrochloric acid, so that "...the hydrogen chloride produced during the combustion of fossil fuels or incineration of solid waste apparently lasts too short a time in the un-reacted state to pose a significant health risk" (WHO, 1982, p. 77)

3.2 Subchronic and Chronic Effects

The major effect of long-term exposure to HCl is dental erosion and discolouration of the teeth. Bleeding of the gums and nose has also been reported as a chronic effect (Cheminfo, 1996; WHO, 1982). In a chronic inhalation study reported by the US EPA (1997) rats exposed to a time-adjusted HCl concentration of 2,500 $\mu\text{g}/\text{m}^3$ for their lifetimes showed extra-thoracic and tracheo-bronchial effects. From this study the US EPA calculated a Lowest Observed Adverse Effect Level (LOAEL) adjusted to Human Equivalent Concentration (LOAEL-HEC) of 6,100 $\mu\text{g}/\text{m}^3$. In another study reported by the US EPA (1997), rats and mice were exposed for 90 days for 6 hours a day, 5 days a week, to three different HCl concentrations (15,000, 30,000 or 75,000 $\mu\text{g}/\text{m}^3$). Only mild respiratory problems were reported, with a slightly greater effect on mice. Calabrese and Kenyon (1991) have suggested a 24-hour Time Weighted Average (TWA) value of 150 $\mu\text{g}/\text{m}^3$ based on the irritant effects of HCl.

3.3 Developmental and Reproductive Effects

Developmental effects were found in rats exposed at 450,000 $\mu\text{g}/\text{m}^3$. However, this level was also toxic to the dams (Cheminfo, 1996).

3.4 Genotoxicity

Hydrogen chloride has produced mutagenic effects in one bacterial test (*E. coli*), in fruit fly, grasshopper and in-vitro hamster lung cells. Negative results occurred in another in-vitro test (SHE

cells). Cheminfo (1996) notes that the significance of these results is not clear since altered acidity in cells and organisms can cause abnormal cell growth.

3.5 Carcinogenicity

There have been several epidemiological studies that have looked at the link between HCL exposure and cancer (Cheminfo, 1996). In one study there was an increased rate of lung cancer. In three cases where controlled studies were conducted there was no evidence of an association with lung, brain or kidney cancer. The New Jersey Dept. of Health and Senior Services indicates that there is limited evidence illustrating that workers who are manufacturing HCL have an increase rate of respiratory cancers (NJDHSS, 1997). IARC has determined that there is inadequate evidence for carcinogenicity in humans and in animals. The overall classification of the compound is Group 3: not classifiable (Cheminfo, 1996). The US EPA has not classified HCL with respect to its potential carcinogenicity (US EPA, 1997).

3.6 Environmental Effects

Insufficient data are available to evaluate the effects of hydrogen chloride on terrestrial wildlife. Pigeons exposed to 150 mg/m³ for six hours per day for 50 days showed symptoms of eye and nose irritation as well as a slight decrease in haemoglobin concentration (Environment Canada, 1984). Tomatoes exposed to 600 µg/m³ hydrogen chloride for eight hours a day for six days demonstrated a 16% reduction in photosynthesis (Godish et al, 1970). Foliar injury was observed in tomato plants exposed to 1.5 mg/m³ for 20 minutes (Grannet, 1976).

Hydrogen chloride is moderately toxic to aquatic organisms. An acute 96-hour LC₅₀ value of 282 mg/L was determined for mosquito fish (*Gambusia affinis*) (Environment Canada, 1984). For aquatic invertebrates, 48-hour LC₅₀ values range from 100 mg/L for shrimp to 1,000 mg/L for cockle (Environment Canada, 1984).

4.0 Existing Ambient Air quality Criteria

4.1 Overview

Currently, the ambient air quality criterion for hydrogen chloride in Ontario is 40 µg/m³ with a 24-hour averaging time. The half-hour Point of Impingement (POI) standard is 100 µg/m³. These were set to prevent corrosion (MOEE, 1994a). The air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of

Environmental Medicine and the Canadian Federal Government have been reviewed. A brief summary is presented in Table 1. Additional details are provided in Section 11.0.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE typically uses a factor of 15 to convert from guidelines based on annual average concentrations to half-hour point-of-impingement limits, and a factor of 3 to convert from guidelines based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality guidelines based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

For hydrogen chloride (and other strongly acidic or strongly alkaline substances) corrosive, odour and irritation effects are the main concern. While the short-term guidance concentration of $150 \mu\text{g}/\text{m}^3$ used by the state of New York is derived from the US EPA, the method used for its derivation is not apparent. The State of New Jersey has calculated a 1-hour acute exposure value of $60 \mu\text{g}/\text{m}^3$, which is used as a screening level where the department will look into the application more closely before issuing a permit (Dresser, 1997). The state of California is proposing to revise its acute Reference Exposure Level (REL) for hydrochloric acid of $3000 \mu\text{g}/\text{m}^3$ (1-hour average) to $2,100 \mu\text{g}/\text{m}^3$. The REL is used to assess the relative risk associated with community exposure resulting from emissions from a particular source.

For their longer term guidelines individual states have used the US EPA Inhalation Reference Concentration (RfC), which is based on irritation and the prevent injury to the upper respiratory system. The US EPA has recently revised its RfC from $7 \mu\text{g}/\text{m}^3$ to $20 \mu\text{g}/\text{m}^3$. Some of the states have already adjusted their criterion to reflect this change and others are expected to follow suit. However, the Commonwealth of Massachusetts continues to consider $7 \mu\text{g}/\text{m}^3$ as a more appropriate value, as they feel an additional safety factor of three is warranted to account for the lack of chronic toxicity studies. None of the agencies reviewed consider HCl a substance with carcinogenic potential, therefore no carcinogenicity risk assessment has been performed.

Table 1. Summary of Existing Air Quality Guidelines¹ for Hydrogen Chloride

Agency	Guideline Value	Basis of Guideline	Date ²	Comments
US EPA (IRIS)	20 µg/m ³ (lifetime daily exposure)	Rat chronic lifetime inhalation RfC - Nasal mucosa hyperplasia	1995	Inhalation Reference Exposure Level for evaluation of non-cancer risk.
California (CAPCOA)	7 µg/m ³ (annual average; may be revised to 20 µg/m ³) FOR: Hydrochloric acid	Reference concentration	1993	Non-cancer Reference Exposure Level. Chronic annual.
	3,000 µg/m ³ (1-hour average) Proposed:	Human irritation concentration	1989	Non-cancer Reference Exposure Level
	2,100 µg/m ³ (1-hour average) FOR: Hydrochloric acid		1998	
Massachusetts (DEEP)	7 µg/m ³ (Annual average)	Reference concentration	1995	Non-cancer Ambient Air Level; US EPA
	7 µg/m ³ (24-hour ceiling limit)	Reference concentration	1995	Threshold Effect, non-cancer Exposure Limit
Michigan (DE)	20 µg/m ³ (24-hour average)	Reference concentration	1995	Non-cancer Screening level for a 24-hour averaging time
New Jersey (DEEP)	7 µg/m ³ (maximum annual average; may be revised to 20 µg/m ³)	Reference concentration	1994	Non-cancer Ambient Reference Concentration
	60 µg/m ³ (acute 1-hour)	Reference concentration	1994	Non-cancer Ambient Reference Concentration
New York (DEC)	7 µg/m ³ (AGE, annual average; may be revised to 20 µg/m ³)	Reference concentration	1990	Chronic annual guideline; US EPA
	150 µg/m ³ (SAC, 1-hour average)	Reference concentration	1990	US EPA
WHO	none		1987	No value found
The Netherlands	none		1992	No value found
Sweden	none		1993	No value found
Canada (CEPA)	none		1993	Not in PEL-1 or PEL-2
Ontario (MOE)	100 µg/m ³ (half-hour average)	Corrosion considerations	1988	Half-hour averaging time: Point of Impingement
	40 µg/m ³ (24-hour average)	Corrosion considerations	1988	24-hour averaging time: Ambient Air Quality Criteria

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

The American Conference of Governmental Industrial Hygienists (ACGIH) has developed a threshold limit value of $7,500 \mu\text{g}/\text{m}^3$ for workplace exposure. The Occupational Safety and Health Administration (OSHA) has established the same value as a *Permissible Exposure Limit* (PEL), "to which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect." (McCloskey, 1988).

4.2 Evaluation of Existing Criteria

There are very little solid data on the chronic or subchronic effects of hydrogen chloride in humans or animals. The US EPA RfC is an estimate of a daily inhalation exposure of the human population that is likely to be without an appreciable risk of deleterious effects, other than cancer, during a lifetime. The RfC for HCl is based on the study by Sellakumar *et al.* (1985). This paper reports details of a previous study (Albert *et al.*, 1982) where 100 rats were exposed to $15,000 \mu\text{g}/\text{m}^3$ for 6-hours a day 5-days per week, which was adjusted to a time-adjusted HCl dose of $2,500 \mu\text{g}/\text{m}^3$. Examination of the nasal mucosa found a slight increase in epithelial or squamous hyperplasia and squamous metaplasia. Since the observed changes in the upper respiratory tract of the exposed rats were minor, the EPA considered this concentration as the LOAEL and calculated a human equivalent LOAEL (HEC) of $6,100 \mu\text{g}/\text{m}^3$. The EPA applied an uncertainty factor of $300 - 3$ for interspecies differences, 10 to account for sensitive sub-populations and 10 for extrapolation from a LOAEL to a No Observed Adverse Effect Level (NOAEL) to derive an RfC of $20 \mu\text{g}/\text{m}^3$ (US EPA, 1997).

The overall confidence in the RfC is noted as low (US EPA, 1997). Low confidence was cited for the study on which the RfC was based, since the study involved only one dose and limited toxicological measurements. The confidence in the database is also low, the supporting data consists of two subchronic bioassays but no additional chronic or reproductive studies are available. However, the US EPA notes that due to the expected portal-of-entry effect of HCl, an additional factor, to take into consideration the lack of second-species chronic bioassay and reproductive bioassay, is not necessary. It also notes that a "Workshop on Health Effects of HCl in Ambient Air", which concludes that a reasonable estimate of the NOAEL in humans would be between 300 and $3000 \mu\text{g}/\text{m}^3$ (Kamrin, 1992, as cited in US EPA, 1997).

The long-term guidelines developed by the agencies reviewed all use the US EPA's RfC as the basis for their limits. Most use the old RfC of $7 \mu\text{g}/\text{m}^3$, however, Michigan has modified its 24-hour screening level to $20 \mu\text{g}/\text{m}^3$ to reflect the change in the RfC established by the EPA. California, New Jersey and New York are all likely to review their criteria based on the new RfC (Alexeef, 1997; DeSantis, 1997; Dresser, 1997). Massachusetts uses an additional uncertainty factor of 3 to take into account the low confidence in the RfC (see Appendix 9.3 for details). If Massachusetts follows its 1994 procedures, their reference concentration would remain unchanged at $7 \mu\text{g}/\text{m}^3$. Given the toxicological effects of low level exposure to HCl are localised rather than systemic, the Ministry does not consider this extra factor is necessary.

The state of California has derived its proposed acute (one-hour) reference exposure level (REL) using the 45 minute NOAEL of 1.8 ppm (2,700 µg/m³) from a study by Stevens *et al.* (1992). Since this study involved humans from a sensitive sub-population, no uncertainty factors were used, but the exposure level adjusted to a one-hour duration, giving the proposed REL of 2,100 µg/m³ (OEHHA, 1998).

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including hydrogen chloride, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies the Ministry had considered appropriate for the development of air quality standards; and technical or economic impacts that may be anticipated as a consequence of the potential revision of the air quality standards.

During the consultation period the Ministry received three submissions from various stakeholders regarding the draft document for hydrogen chloride. Comments from a utility stakeholder indicated that adequate chloride content was crucial in enhancing the removal of elemental mercury in fuel burning with conventional control devices. They requested that a balance between the emissions of HCl and mercury be taken into account when setting air quality standards for HCl. Comments from a rubber industry stakeholder indicated that emissions of hydrogen chloride was a result of flaring of methyl chloride in rubber manufacturing processes to reduce the explosive potential of the latter compound. Therefore, a balance between the emissions of HCl and methyl chloride should be considered in revising air quality standards for HCl. The utility stakeholder and stakeholders from the automotive manufacturing industry commented on the appropriateness of the RfC of US EPA and on the animal study from which the toxicity value for Ontario's air quality standards for hydrogen chloride were derived. These stakeholders pointed out that data from available human studies suggested a higher range of toxicity thresholds for HCl.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (Information Drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard, which are presented in Section 8.0 below. This is the next phase in the

overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for HCl.

7.0 Considerations in the Development of Air Quality Standards for Hydrogen chloride

The existing ambient air quality criterion for HCl in Ontario is $40 \mu\text{g}/\text{m}^3$ (24-hour average), while the point of impingement standard is $100 \mu\text{g}/\text{m}^3$. Both values are based on corrosion as a limiting effect.

Hydrogen chloride is a strong irritant to the eyes, mucous membranes, and the skin. In one controlled human exposure study, asthmatics exposed to levels between $1,200$ and $2,700 \mu\text{g}/\text{m}^3$ for 45 minutes showed no apparent exposure-related effects on subjective symptoms or pulmonary function. The State of California has proposed a one-hour acute REL of $2,100 \mu\text{g}/\text{m}^3$ based on this study.

The RfC of $20 \mu\text{g}/\text{m}^3$ developed by the US EPA is based on studies in rats, which demonstrated cellular effects indicative of irritation in the respiratory system at exposure concentrations of $15,000 \mu\text{g}/\text{m}^3$. The Ministry reviewed the results of the 1990 Workshop on the Health Effects of HCl in Ambient Air (Kamrin, 1992). The Ministry concurs with the US EPA, that due to the limited data on HCl, the conclusions from this conference are not adequate for developing a standard. The RfC incorporates adjustments for exposure duration, differences in respiratory physiology between rats and humans and a combined uncertainty factor of 300. The Ministry concurs with the US EPA that the uncertainty factors used are reasonable and that the resulting RfC is protective of human health.

Reported odour thresholds vary from a low of $100 \mu\text{g}/\text{m}^3$ to a high of $7,800 \mu\text{g}/\text{m}^3$. The highly irritating nature of HCl suggests that odour is not the limiting factor for setting an ambient air quality standard. A review of data available on the effects of HCl on terrestrial plants conducted by the Ministry suggests that $60 \mu\text{g}/\text{m}^3$ (30 day average concentration) would not result in any adverse impacts (Harper, 1988).

In light of the corrosive nature of HCl, the reported odour thresholds, and potential toxicity to plants, the ministry does not consider the proposed one-hour acute REL of $2,100 \mu\text{g}/\text{m}^3$ from the State of California as appropriate for the basis for the POI derivation.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies worldwide. Of the criteria reviewed, the Ministry has evaluated the scientific studies which support the development of the RfC by the US EPA reasonable. After reviewing additional toxicological information, the Ministry has considered that it is reasonable to derive a 24-hour AAQC for HCl based on this RfC of $20 \mu\text{g}/\text{m}^3$. Based on dispersion modelling, a calculated half-hour POI of $60 \mu\text{g}/\text{m}^3$ can be derived. In light of the corrosive nature of HCl and comments from stakeholders, the Ministry has decided to maintain the current value of $100 \mu\text{g}/\text{m}^3$ as the POI standard.

The Ministry has recommended to revise the 24-hour AAQC to $20 \mu\text{g}/\text{m}^3$ from the current value of $40 \mu\text{g}/\text{m}^3$ for HCl. These air quality standards of HCl are considered to provide sufficient protection for human and environmental health.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and stakeholders' comments, the Ministry is proposing the following Ambient Air Quality Criterion and half-hour Point Of Impingement standard for hydrogen chloride:

- a 24-hour average AAQC of $20 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for hydrogen chloride based on the adverse health effects of this compound; and,
- a half-hour POI of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for hydrogen chloride based on the corrosive effect of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes

-
- timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed

that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for HCl can be sent to:

Jim Smith
Director, Standards Development Branch
Ontario Ministry of the Environment
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Michigan Department of Natural Resources, 1995/1997. Air Toxics Screening Levels. Air Quality division. 6 p. + Appendices.

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New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 p. + Appendices.

New Jersey Department of Health and Senior Services (NJHSS), 1997. Hydrogen Chloride - Hazardous Materials Data Sheet. Right to Know Program, Trenton, NJ.

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Sellakumar, A.R., C.A. Snyder, J.J. Solomon and R.E. Albert. 1985. Carcinogenicity for Formaldehyde and Hydrogen Chloride in Rats. *Toxicol. Appl. Pharmacol.* **81**: 401-406.

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. There is a reference concentration for chronic exposure (RfC) of 20 $\mu\text{g}/\text{m}^3$ in the IRIS database (US EPA, 1997 last review 07/01/95). There is no carcinogenicity assessment for HCl due to a lack of data.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

Key Reference(s):

Sellakumar, A.R., C.A. Snyder, J.J. Solomon and R.E. Albert. 1985. Carcinogenicity for Formaldehyde and Hydrogen Chloride in Rats. *Toxicol. Appl. Pharmacol.* 81: 401-406.

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6. *Peer Review Process and Public Consultation:*

In its assessment, the US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

No guidelines exist. The risk estimate discussed is for respiratory exposure from air only.

8. Key Risk Assessment Considerations:

The US EPA (1997) has calculated an RfC which represents risk from adverse effects other than cancer. It is an estimate of the daily exposure of a segment of the human population that is likely to be without appreciable risk to HCl during a lifetime. This RfC was calculated using results from two documents addressing the same inhalation exposure study in rats (Sellakumar *et al.*, 1985 and Albert *et al.*, 1982). One hundred male Sprague-Dawley rats were exposed to 10 ppm (15,000 $\mu\text{g}/\text{m}^3$) for 6 hours a day, 5 days a week. Based on the results of histologic section analysis, necropsies and other histopathological events, a Lowest Observed Adverse Effect Level (LOAEL) of 15,000 $\mu\text{g}/\text{m}^3$ was calculated. This LOAEL was converted to a Human Equivalent Concentration (HEC) of 6,100 $\mu\text{g}/\text{m}^3$. The critical effects considered were a 10 % increase in epithelial or squamous hyperplasia in the nasal mucosa, four additional animals with squamous metaplasia and a 24% incidence of hyperplasia of the laryngeal-tracheal segment in HCl exposed rats.

An uncertainty factor of 10 was applied to allow for intraspecific differences, an additional factor of 10 was applied to account for the extrapolation from a LOAEL to a NOAEL, and a factor of 3 was used to account for the interspecies differences. The EPA states that because of the portal-of-entry effect of HCl, it was not necessary to use an additional uncertainty factor that would cover the lack of a second-species chronic bioassay and a reproductive bioassay. The inhalation RfC calculated was 20 $\mu\text{g}/\text{m}^3$ (6,100 $\mu\text{g}/\text{m}^3 / 300$). The EPA points out that a value of 300 to 3,000 $\mu\text{g}/\text{m}^3$ has been proposed as a reasonable estimate of human NOAEL for HCl (Kamrin, 1992). This estimate is the result of an expert review workshop based on examination of the HCl literature, the comparison with sulphuric acid toxicity and the professional judgement of those present at the workshop. Because the workshop did not address the area of uncertainty stated by EPA, the Agency decided that the use of an uncertainty factor was appropriate. However, the EPA places a low confidence in this RfC because the principal research, the chronic study, used only one dose and limited toxicological measurements and because the data base does not provide strong additional chronic and reproductive studies.

The EPA reports that the only available controlled human exposure study of HCl showed no exposure-related effects of HCl when ten asthmatic humans (five of each sex) were exposed to 1.2 or 2,700 $\mu\text{g}/\text{m}^3$ of HCl for 45 minutes (Stevens *et al.*, 1992). An animal study involving baboons suggests that the exposure to higher doses, up to 15,000,000 $\mu\text{g}/\text{m}^3$ for a short time (15 minutes) does not produce permanent effects to the respiratory system (Kaplan *et al.*, 1988). Because baboons and humans possess a more complex structure of their upper airways than rodents, it is suggested that humans are probably much less sensitive to HCl than mice. From a 1974 study, it appears that mice are two to three times more sensitive than rats to HCl exposure (Darmer *et al.*, 1974). The EPA reports two studies from the same lab dealing with effects on reproduction and development of mice after inhalation of 450,000 $\mu\text{g}/\text{m}^3$ HCl for one hour (Pavlova, 1976 and GAMBIT Technologies, Inc., 1981). At this concentration, mouse reproduction and development are affected. Mortality occurred in

one third of the adults and foetal mortality was significantly higher. Also reported was a decrease in the number of live foetuses, a decrease in foetal weight and an increase of lung weight.

The EPA reports that HCl gas concentrations of 75,000 to 150,000 $\mu\text{g}/\text{m}^3$ are tolerable for one hour, while concentrations ten times higher are dangerous even for brief periods. More prolonged or higher concentrations will cause death. Mists of HCl are considered less harmful than anhydrous hydrochloric acid because of the absence of dehydration action (Sax, 1995). Inhalation of hydrogen chloride may cause coughing and choking, and inflammation and ulceration of the respiratory tract, while concentrated solutions can cause severe burns and even permanent eye damage (Rumack, 1975-present). Occupational exposures have led to dermatitis, photosensitization (Merck, 1983), gastritis and chronic bronchitis (ACGIH, 1980).

All references in above paragraphs as cited in US EPA (1997).

9. *Key Risk Management Considerations:*

None, since no guidelines for ambient air exist.

10. *Multimedia Considerations of Guidelines:*

None are reported.

11. *Other Relevant Factors:*

IRIS shows no data for carcinogenicity of hydrogen chloride.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The reference concentration (RfC) of $7 \mu\text{g}/\text{m}^3$ is to be used for assessing chronic non-cancer risks of hydrogen chloride. This exposure level will most probably be raised to meet the new EPA RfC value of $20 \mu\text{g}/\text{m}^3$ during the next revision process, in the next 6 months (Alexeeff, 1997). The reference level for acute exposure is $3,000 \mu\text{g}/\text{m}^3$. A revised value of 2,100 is being proposed. Chronic exposure reference levels should be compared with modelled annual average air concentrations, while acute non-cancer reference levels should be compared with modelled 1-hour average concentrations.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritised. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility with another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimise revisions and resubmission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Hydrochloric Acid. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

Lewis, DC and G. V. Alexeeff, 1989. Quantitative Risk Assessment of Non-cancer Health Effects for Acute Exposure to Air Pollutants. In: Proceedings of the Air and Waste Management Association 82nd Annual Meeting, June 1989, Vol. 89-91.4p.

Alexeeff, G.V., 1997. Personal communication.

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site-specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

Current, but updates using new California risk assessment guidelines are being considered in the California Senate. It is most likely that the chronic guideline will be raised to 20 $\mu\text{g}/\text{m}^3$ to reflect the new RfC from the EPA. (G. Alexeeff, CAL-EPA, personal communications, 01/97 and 02/97). A Scientific Panel Review Draft for the determination of an acute toxicity exposure level was released in October 1998.

8. Key Risk Assessment Considerations:

California did agree with the 1991 EPA's RfC of 7 $\mu\text{g}/\text{m}^3$ as its Reference Exposure Level (chronic). However, the IRIS RfC value for hydrogen chloride has been updated in July 1995, after the CAPCOA guidelines were adopted. It went from 7 $\mu\text{g}/\text{m}^3$ in 1991 to 20 $\mu\text{g}/\text{m}^3$ in 1995 (US EPA, 1997).

The non-cancer acute reference exposure level for inhalation of 3,000 $\mu\text{g}/\text{m}^3$ is based on human respiratory irritation using the Defined Practical Threshold (DPT) methodology proposed by Lewis and Alexeeff (1989). It is a log-probit modelling of human irritation dose-response data integrating as many data sets as available. The benchmark dose is estimated using maximum likelihood procedure for a 1 % increase in toxic response with 95 % lower confidence limit on dose. The obtained value should protect against perceptible occurrence of observable effects, including irritation, among an exposed human population for a one-hour exposure period.

The proposed acute (one-hour) reference exposure level (REL) has been derived using the 45 minute NOAEL of 1.8 ppm (2,700 $\mu\text{g}/\text{m}^3$) from a study by Stevens *et al.* (1992). Since this study involved humans from a sensitive sub-population, no uncertainty factor were used, but the exposure level adjusted to a one-hour duration giving the proposed REL of 2,100 $\mu\text{g}/\text{m}^3$ (OEHHA, 1998).

9. Key Risk Management Considerations:

The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in screening risk assessments to determine the maximum offsite cancer risk for exposed human population. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of hydrogen chloride emission control. It appears that the options are under local control and are based on local risk, socio-economic analyses and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels.

10. Multimedia Considerations of Guidelines:

In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993). Hydrogen chloride is not one of the substances requiring non-inhalation modelling.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

Both the Threshold Effects Exposure Limit (TEL; 24-hour average) and the Allowable Ambient Limit (AAL; annual average) are $7 \mu\text{g}/\text{m}^3$. It is stated in the latest revised edition (1995) that "in cases where the TEL equals the AAL, the TEL concentration and averaging time should be used." The EPA's new RfC value of $20 \mu\text{g}/\text{m}^3$ will not necessarily be adopted in the updated version (December 1997), because of disagreement in uncertainty factors between the EPA and ORS (Diane Manganaro, ORS, 97/02/18).

4. *Application:*

"...the Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) Decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 p.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated List of 24-hour Average Threshold Effects Exposure Limit (TEL) Values and Annual Average Allowable Ambient Limit (AAL) Values.

Key Reference(s):

US EPA, 1994. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, D.C.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature, were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was employed. As guidelines, the process used and values generated are not subjected to the extensive review and consultation that air quality standards would be subjected to. Nonetheless, external peer reviews were carried out, and public input was solicited through at least two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE staff, 1996). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each AAL will undergo review a minimum of every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

For hydrogen chloride, the Massachusetts Department of Environmental Protection agrees with the old US EPA's RfC of $7 \mu\text{g}/\text{m}^3$ as its Allowable Ambient Limit (AAL) and its Threshold Effects Exposure Limits (TEL). TELs are exposure limits based on threshold health effects while AALs are based on both threshold and non-threshold health effects. The DEP's decision to incorporate the RfCs permits a way to consider "recent peer-reviewed toxicity information on the threshold effects of a compound while maintaining the same degree of health protection afforded by the CHEM/AAL methodology." (ORS, 1994). Because hydrogen chloride is not considered as a carcinogen, (non-threshold exposure limit equals 1) both AAL and TEL are set to $7 \mu\text{g}/\text{m}^3$. However, the note attached to the revised list mentions specifically that "in cases where the TEL equals the AAL, the TEL concentration and averaging time should be used".

It is uncertain that the updated AAL and TEL will be revised to follow the EPA's new RfC of $20 \mu\text{g}/\text{m}^3$ during the next revision process (possibly in December 1997). ORS (1994) stated that in 1991, the EPA did not follow the recommended procedure while formulating the uncertainty factors for hydrogen chloride. The EPA used a factor of 10 for dosimetric adjustment instead of a factor of 3 as it did for other gases such as sulphur dioxide. In addition, ORS felt that a factor of 3 was to be added to account for the low confidence that the EPA placed in the database, specifically: only one dose used in the chronic study, limited toxicological measurements and absence of properly conducted chronic and reproductive studies (ORS, 1994 and D. Manganaro, ORS, personal communication, 1997/02/18). In 1991, the EPA used a dose of $6,500 \mu\text{g}/\text{m}^3$ and an uncertainty factor of 1000, which led to a RfC of

6.5 $\mu\text{g}/\text{m}^3$, ORS used the same dose value and an uncertainty factor of 900 which led to a RfC of 7.2 $\mu\text{g}/\text{m}^3$. Both values become, after rounding, 7 $\mu\text{g}/\text{m}^3$. However, in the 1997 IRIS database, the EPA has used a factor of 3 for the dosimetric adjustment, as recommended by the ORS but did not use an additional factor of 3 to account for the low confidence in its value. The final uncertainty factor, applied to a dose of 6,100 $\mu\text{g}/\text{m}^3$ (it changed from 6,500 to 6,100 without explanation, even if the same study was used) was 300 to give a RfC of 20 $\mu\text{g}/\text{m}^3$. If ORS follows its procedure of 1994, the uncertainty factor would continue to be 900, which would give a RfC of 7 $\mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effects reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

10. Multimedia Considerations of Guidelines:

Before the current revised methodology, a factor of 20% was systematically applied as a relative source contribution factor. However, the 1994 revision states that "the multimedia exposure factor is not used with water soluble gases (i.e., NH_3 , H_2S and HCl) since it is assumed that exposure to these compounds is largely via inhalation and they are mainly respiratory toxicants." (ORS, 1994).

11. Other Relevant Factors:

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* Michigan

3. *Guideline Value(s):*

The screening levels (Initial Threshold Screening Level; ITSL) in Michigan is $20 \mu\text{g}/\text{m}^3$ based on a 24-hour averaging time.

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxic rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. The maximum ambient concentration of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

Michigan Department of Natural Resources, 1995/1997. Air Toxics Screening levels. Air Quality division. 6 p. + Appendices.

Key Reference(s):

US EPA, 1997. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, D.C.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months, while a complete list of all screening levels is published once a year.

8. *Key Risk Assessment Considerations:*

When the EPA has established a RfC, it is used to define the ITSL. For hydrogen chloride, Michigan agrees with the US EPA's RfC of $20 \mu\text{g}/\text{m}^3$ because it is not considered to be a carcinogen. For other chemicals, different agencies can be used to obtain reference screening levels.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No Information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* New Jersey

3. *Guideline Value(s):*

The reference concentration for inhalation in New Jersey is $7 \mu\text{g}/\text{m}^3$ to be compared with long-term (annual) ambient air concentrations. However, it is expected that the value will be raised shortly to $20 \mu\text{g}/\text{m}^3$ (Alan Dresser, NJDEP, 97/02/18, personal communication). The New Jersey Department of Environmental Protection (NJDEP) has also calculated a one-hour reference concentration based on acute exposure to be $60 \mu\text{g}/\text{m}^3$.

4. *Application:*

The list of reference concentrations for inhalation is maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. The reference concentrations do not appear to be legally enforceable since the Air Quality Permitting Program Risk Management Committee can issue a final case-by-case review and recommendation regarding permitting of the source after it has failed a first- and a second-level risk screening. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.). However, if the hazard index calculated is higher than one, the risk is evaluated on a case-by-case basis.

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 p. + Appendices.

Updated reference concentrations for 1997 have just been issued by the NJDEP staff.

Key Reference(s):

US EPA, 1997. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, D.C.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. Key Risk Assessment Considerations:

In the case of non-carcinogens, the RfC is used directly in the risk assessment or screening procedures. For hydrogen chloride, New Jersey agreed with the US EPA's old RfC of $7 \mu\text{g}/\text{m}^3$ and with the new value of $20 \mu\text{g}/\text{m}^3$. For other chemicals, different agencies can be used to obtain reference concentrations. However, the NJDEP has calculated its own 1-hour acute exposure value of $60 \mu\text{g}/\text{m}^3$ without other information on the rationale for this value, it is used as a check point at which the department will look into the application more closely before issuing a permit (A. Dresser, personal communication, 97/02). New Jersey believes that a chemical is not proven to be non-carcinogenic just because no carcinogenicity has been demonstrated. There is no information in US EPA IRIS regarding the carcinogenicity of hydrogen chloride, so no conclusion can be reached on its carcinogenicity at the present time.

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC; 1-hour average air concentration) is $150 \mu\text{g}/\text{m}^3$ and the current Annual Guideline Concentration (AGC) is $7 \mu\text{g}/\text{m}^3$, but it is expected to be modified as $20 \mu\text{g}/\text{m}^3$ in a few months (S. DeSantis, N.Y. DEC, Personal communication, January 1997).

4. *Application:*

"... the guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (N.Y. DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

The guide is in a revision process and actual values can only be obtained verbally, no documents are presently available.

Key Reference(s):

American Conference of Governmental Industrial Hygienists (ACGIH), 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

6. *Peer Review Process and Public Consultation:*

The scientific documents prepared by the New York State employed peer-reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guideline development process, but specific information on the process for hydrogen chloride was not presented in the available documentation.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The actual AGC value reflects the revised EPA's RfC. In the previous edition of Air guide-1 (1991), the AGC was $7 \mu\text{g}/\text{m}^3$ as was the RfC at the time. The SGC has not been modified.

New York State (1991) has classified the toxicity of hydrogen chloride as low. Compounds given the designation of low are "those chemicals that might cause irritation or reversible effects to sensitive members of the population, and which do not meet the criteria for classification as HIGH or MODERATE toxicity contaminants". The short-term guideline concentration for this class of chemicals was under review in 1991 and no additional information is available on the procedure used to derive the actual concentration. It is stated, however, that both the short-term and the long-term guidelines for hydrogen chloride are derived from the EPA sources. No additional information is given as to the actual process followed to reach the current guideline value.

9. Key Risk Management Considerations:

A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses as employed in the permitting process. Presently, the latest version of Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

No information.

11.7 Agency-Specific Summary: World Health Organisation (WHO)

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* World Health Organisation

3. *Guideline Value(s):*

Not on the list of substances considered by the guidelines.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No.

23. World Health Organisation, Regional Office for Europe, Copenhagen, Denmark, 426 p.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Hydrogen chloride does not appear on the list of environmental quality objectives nor is it mentioned in the emission regulations.

4. *Application:*

None.

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A Review of Environmental Quality Objectives and Their Policy Framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 p.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No specific information on this issue was presented in the available English documentation.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. A specific schedule for revisions based on this process has not been announced and hydrogen chloride is not on the initial list of chemicals to be considered.

11. *Other Relevant Factors:*
No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* According to Dr. K. Victorin of the Swedish Institute of Environmental Medicine (personal communication, January 1997), no official Swedish air quality guidelines have been promulgated by the Swedish Environmental Agency.

3. *Guideline Value(s):*

No information.

4. *Application:*

No information.

5. *Documentation Available:*

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. *Chemosphere* 27: 1691-1706.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.10 Agency-Specific Summary: Federal Government of Canada

1. *Name of Chemical:* Hydrogen chloride

2. *Agency:* Canadian (CEPA)

3. *Guideline Value(s):*

No information.

4. *Application:*

No information.

5. *Documentation Available:*

Not on the Canadian Environmental Protection Act (CEPA) Priority Substances List

Key Reference(s):

No information.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram
MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic

MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or <i>Ontario Ministry of Environment and Energy</i>
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences (USA)</i>
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program (USA)</i>
OEHHA	<i>Office of Environmental Health Hazard Assessment (California EPA)</i>
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either <i>Reference Exposure Level</i> as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or <i>Recommended Exposure Limit</i> used by both NIOSH and ATSDR
RF	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration (New York State)</i>
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

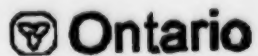




**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
ISOPROPYL BENZENE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised October, 1999, identified candidate substances for which air standards will be reviewed over the next several years. Isopropyl benzene was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1979. A review of scientific and technical information relevant to setting an ambient air quality standard for isopropyl benzene has previously been provided to stakeholders for comment. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour Point of Impingement (POI) standard for isopropyl benzene.

Isopropyl benzene, also commonly referred to as cumene, is a colourless liquid with a sharp, penetrating odour. It is derived from the distillation of coal tar, naphtha, and petroleum. Isopropyl benzene is used mainly as an intermediate for the production of phenol, acetone, and alpha-methyl styrene, which are components widely used in plastic resins. Another use of isopropyl benzene is as an additive to aviation gasoline to improve the octane rating. It is also a constituent of cumen oil which is used as a solvent and a thinner for paints and enamels.

Isopropyl benzene is not miscible with water and tends to stay on the surface until it evaporates. Soil studies show that isopropyl benzene is biodegraded rapidly by micro-organisms under aerobic conditions. In the atmosphere, isopropyl benzene exists mostly in the vapour phase where it persists for a few days and is then destroyed through photochemical reactions.

The atmospheric emissions of isopropyl benzene, in Canada and in Ontario between 1993 and 1995, did not indicate any consistent trend. In Canada, releases of isopropyl benzene between 1993 and 1995 ranged from 24.7 to 91 tonnes. In the same period, atmospheric releases in Ontario ranged from 7 to 10 tonnes. In 1997, reported atmospheric releases in Canada and in Ontario amounted to 26.4 tonnes and 6.4 tonnes, respectively. Emissions from petroleum refineries accounted for most of the releases in Ontario. Isopropyl benzene is also released by gasoline stations and through emissions from motor vehicles.

Environment Canada measured isopropyl benzene concentrations at four Metropolitan Toronto locations. This agency found that approximately half of the samples were below the $0.05 \mu\text{g}/\text{m}^3$ detection limit, the highest concentration observed was $0.37 \mu\text{g}/\text{m}^3$. Half-hourly monitoring performed by the MOE indicated measured isopropyl benzene concentrations of up to $4.8 \mu\text{g}/\text{m}^3$ in ambient air near landfills in the greater Toronto area, and $22 \mu\text{g}/\text{m}^3$ near an asphalt plant in Vineland.

Isopropyl benzene is not a significant health threat at low concentrations. It has an extremely low odour threshold and its vapours are very irritating. Exposure through inhalation can cause dizziness, light-headedness, and fainting. Contact with isopropyl benzene can irritate the eyes, nose, mouth, and throat, and may also cause skin rashes. Exposure to skin occurs mainly in occupational settings.

The current Ontario half-hour POI guideline and the 1-hour AAQC are both set at $100 \mu\text{g}/\text{m}^3$. This value has been developed on the basis of the odour nuisance property of isopropyl benzene. In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, the Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Three U.S. agencies have developed air quality criteria for isopropyl benzene on the basis of its health effects. A 24-hour criteria of $87 \mu\text{g}/\text{m}^3$ was developed by the State of Michigan, while annual criteria of 9 and $400 \mu\text{g}/\text{m}^3$ were established by New Jersey and the US EPA, respectively.

Of the criteria reviewed from other agencies, the Ministry has evaluated, and accepted the scientific studies which support the development of the RfC established by the US EPA. After reviewing additional toxicological information, the Ministry has considered that the uncertainty factors used to derive the RfC of $400 \mu\text{g}/\text{m}^3$ by the US EPA reasonable. The RfC becomes the health-based 24-hour AAQC of $400 \mu\text{g}/\text{m}^3$. Deriving a half-hour POI from the 24-hour AAQC of $400 \mu\text{g}/\text{m}^3$ will result in a criterion higher than the current POI guideline. Therefore, replacing the odour-based POI of $100 \mu\text{g}/\text{m}^3$ is not recommended. Considering the odour nuisance of isopropyl benzene as a sensitive endpoint, the odour-based 10-min AAQC is maintained.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and considering other relevant information such as the aesthetic effects (i.e., odour nuisance) of isopropyl benzene, the Ministry is proposing the following Ambient Air Quality Criteria and Point Of Impingement standard for isopropyl benzene:

- a 24-hour average AAQC of $400 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for isopropyl benzene based on the adverse health effects of this compound; and,
- an 1-hour average AAQC of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for isopropyl benzene based on the odour nuisance of this compound; and,
- a half-hour average POI standard of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for isopropyl benzene based on odour nuisance and adverse health effects.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Isopropyl benzene was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing guideline in 1979. A review of scientific and technical information relevant to setting an ambient air quality standard for isopropyl benzene had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for isopropyl benzene.

2.0 General Information

2.1 Physical and Chemical Properties

Isopropyl benzene is a colourless liquid with a sharp, penetrating odour. The following list provides some of its properties:

CAS #	98-82-8
RTECS #	GR8675000
UN #	-
Conversion Factors	1 ppm = 4.9 mg/m ³
Boiling Point	152.7°C
Melting Point	-96°C
Henry's Law Constant	-
Flash Point	35-39°C (closed cup)
Specific Gravity	0.86 at 25°C
Water Solubility	50 mg/L at 25°C
Log K _{ow}	3.66
Formula	C ₆ H ₅ CH[CH ₃] ₂
Molecular Weight	120.2
Vapour Density (air = 1)	-
Vapour Pressure	4.6 mmHg at 25°C
Common Synonyms	cumene, 1-methylethyl benzene, 2-phenylpropane

Isopropyl benzene has an extremely low odour threshold and its vapour is very irritating. The odour thresholds for this compound have been reported to range from 39 to 6,370 µg/m³ (Nagy, 1991; Ruth, 1986). The geometric mean odour thresholds has been calculated to be 157 µg/m³ (0.032 ppm) and the geometric mean of the recognition levels is 231 µg/m³ (0.047 ppm) (AIHA, 1989). Odour threshold values for isopropyl benzene and other alkylbenzenes are affected by a fading in the irritation response (desensitization) within the first two minutes of exposure (Nielsen *et al.*, 1988). In occupational settings, the odour threshold only serves as a warning of exposure, skin absorption must also be considered in total worker exposure.

2.2 Uses

Isopropyl benzene is mainly used as an intermediate required for the production of phenol, acetone, and alpha-methyl styrene, which are components widely used in plastic resins (ACGIH, 1991). Another use of isopropyl benzene is as an additive to aviation gasoline to improve the octane rating. It is also a constituent of cumlin oil used as a solvent and a thinner for paints and enamels.

2.3 Sources and Levels

Sources

Isopropyl benzene is derived from the distillation of coal tar, naphtha and petroleum (ACGIH, 1991). It is very volatile, evaporates quickly, and can create a flammable or explosive mixture in air. Sources of isopropyl benzene, in ambient air occur mainly through fugitive emissions from plastic handling, manufacturing and from petrochemical refineries or from industrial discharges and spills. Isopropyl benzene is also released from gasoline stations and through emissions from motor vehicles, as it is a minor component of hydrocarbon fuels (ACQUIRE, 1997).

The National Pollutant Release Inventory (NPRI) of Environment Canada summarizes the emissions of chemicals in Canada based on information provided by reporting facilities (NPRI, 1993; NPRI, 1994; NPRI, 1995 & NPRI, 1996). Data obtained from the 1993 to 1996 NPRI reports indicates that there were fewer than 20 sources that emitted isopropyl benzene in Canada. The annual atmospheric releases of isopropyl benzene were 39.6, 91, 24.7 and 16.4 tonnes in 1993, 1994, 1995 and 1996, respectively. Atmospheric releases as indicated in the last two reporting years had been declining. Over 55 % of the total releases of isopropyl benzene occurred in Ontario, however no consistent pattern of releases was observed in the province. There were 8.9, 10, 7 and 9.1 tonnes of isopropyl benzene released to air in Ontario during 1993, 1994, 1995 and 1996 respectively. Most of the releases in these years can be attributed to the petroleum refinery industries. Furthermore, all of these releases were emitted to air.

From an analysis of recent applications for Certificates of Approval in Ontario, only one facility was identified as emitting isopropyl benzene and the approval was for a paint operations facility. The resulting Ground Level Concentration, estimated by Regulation 346 dispersion modelling for this source was approximately 22 $\mu\text{g}/\text{m}^3$.

Ambient air concentrations

Levels of isopropyl benzene found in occupational settings in industries provide an indication of levels expected in ambient air around these industries. Concentrations measured varied between 60 and 250

$\mu\text{g}/\text{m}^3$ in the vulcanization area of a shoe sole factory, between 2 and 200 $\mu\text{g}/\text{m}^3$ in a tire retreading factory and between 0 and 10 $\mu\text{g}/\text{m}^3$ in a rubber extrusion area (Cocheo *et al.*, 1983). Exhaust concentrations of isopropyl benzene from gasoline fuelled vehicles composed 0.2% of the non-methane hydrocarbons present in the emissions (Nelson and Quigley, 1984).

Environment Canada sampled ambient isopropyl benzene concentrations at 34 urban locations across Canada. In Ontario, isopropyl benzene concentrations were measured at four Metropolitan Toronto locations, between September and December 1995. These concentrations represent the levels obtained from fugitive emissions and motor vehicle emissions at urban locations. Isopropyl benzene concentrations were below the detection limit of 0.05 $\mu\text{g}/\text{m}^3$ in approximately half of the samples. The average concentrations measured ranged from 0.05 to 0.10 $\mu\text{g}/\text{m}^3$, with maximums ranging from 0.13 to 0.37 $\mu\text{g}/\text{m}^3$. These maximum values are all well below the absolute odour perception limit of 39 $\mu\text{g}/\text{m}^3$ (Hellman and Small, 1974). The average ambient concentration of isopropyl benzene has been estimated to be 15 $\mu\text{g}/\text{m}^3$ in different U.S. locations (US EPA, 1987).

Isopropyl benzene monitoring by the MOE indicated that half-hour measurements of up to 4.8 $\mu\text{g}/\text{m}^3$ (detection limit of 0.01 $\mu\text{g}/\text{m}^3$) were obtained in ambient air near landfills in the greater Toronto area in 1994 and 1995, 22 $\mu\text{g}/\text{m}^3$ in 1996 near an asphalt plant in Vineland, and 0.5 $\mu\text{g}/\text{m}^3$ near a petrochemical industry in the Greater Toronto Area (MOEE, 1997).

2.4 Environmental Fate

In the atmosphere, isopropyl benzene is expected to exist mostly in vapour phase. Primary degradation pathways for the petrochemically generated hydroxyl radicals are through photochemical reactions and the half-life of the radicals is estimated to be 1.3 days and 1.6 days at temperatures of 25 °C and 32 °C respectively (Ravishankara *et al.*, 1978). Isopropyl benzene is not miscible with water, and tends to stay on the surface until it evaporates within a few days. In soil, studies show that isopropyl benzene is rapidly biodegraded by micro-organisms under aerobic conditions. Isopropyl benzene is strongly adsorbed in soil and is not significantly mobile in soils. The high vapour pressure of isopropyl benzene (4.6 mm Hg at 25 °C) indicates that volatilisation of isopropyl benzene, from soil surfaces would be significant. Isopropyl benzene is not expected to significantly bioconcentrate in aquatic organisms, as a bioconcentration factor of 35.5 was measured in goldfish (HSDB, 1999). Isopropyl benzene is readily degraded by *Pseudomonas* bacteria (HSDB, 1999).

3.0 Toxicology of Isopropyl Benzene

The following toxicological review of isopropyl benzene is focussed on inhalation exposure, as this is considered the primary route of exposure for humans in Ontario and since the data from the NPRI

indicated that all of the isopropyl benzene generated from industrial sources was emitted to the air. Data on other exposure media are included where relevant, or where inhalation data are lacking.

There are no detailed human toxicity data available for isopropyl benzene (US EPA, 1998). Isopropyl benzene may affect humans through inhalation and is readily absorbed through the skin. Contact can irritate the eyes, nose, mouth, and throat, and it may also cause a skin rash (NIOSH, 1997). Following absorption, isopropyl benzene is metabolised into water soluble compounds, which are readily excreted. This indicates that isopropyl benzene is not likely to accumulate within the body (US EPA, 1998). No epidemiology case reports or clinical control studies in humans were found (US EPA, 1998).

3.1 Acute Toxicity

The toxicological profile of acute effects of isopropyl benzene is similar to those of many solvents which are known to induce central nervous system (CNS) depression. These effects occur at concentrations greater than 500 ppm (2450 mg/m³) (US EPA 1998). Brief exposure (20-min.) of mice to isopropyl benzene at 0, 2000, 4000 or 8000 ppm (0, 9800, 19600 or 39200 mg/m³) induced CNS effects such as decreased arousal and rearing (at ≥ 9800 mg/m³), changes in muscle tone/equilibrium such as changes in grip strength and mobility (at ≥ 19600 mg/m³) and decreases in sensorimotor activity such as decreased tail pinch and touch responses (at ≥ 19600 mg/m³). Rats exposed to isopropyl benzene for 6 hours at 0, 100, 500 or 1202 ppm (0, 490, 2450 or 5900 mg/m³) induced gait (walking) abnormalities and decreased rectal temperatures only at the highest exposure level (1,202 ppm or 5,900 mg/m³) (Cushman *et al.*, 1995 as cited in US EPA, 1998). Decreased activities were found in both sexes at the highest level, but only in females at the 500 ppm (2450 mg/m³) level.

3.2 Subchronic and Chronic Toxicity

In an inhalation exposure study, exposed Fischer 344 rats to isopropyl benzene vapour for 6 hour/day, 5 days/week for 13 weeks at concentrations of 0, 100, 496 or 1202 ppm (0, 492, 2,438 and 5,909 mg/m³) (Cushman *et al.*, 1995 as cited in US EPA, 1998). In a subsequent experiment, which was a repeat of the first experiment, added an additional concentration group (50 ppm or 245 mg/m³) and a four-week post-exposure treatment-free period. Study parameters were: clinical signs of toxicity; body weight; food and water consumption; blood chemistry; gross pathology and histopathology, including all respiratory tissues; neurological functions, e.g. functional observation battery and motor activity. Exposure to isopropyl benzene did not cause neurohistopathological changes in rats. There were significant increases in the weights of the kidneys, adrenal glands and livers at the three high concentrations in both sexes in the first experiment. Some degree of reversibility in organ weight gains was noted in rats given 4 weeks treatment-free period. These alterations in organ weight were considered toxicologically significant and adverse effects because of the limited reversibility and

uncertainty about the progression and fate of these weight changes under chronic exposures. No changes in other organs were observed. Significant haematological changes, such as increases in leukocytes and platelets in both sexes and in lymphocyte in males and significant decreases in erythrocyte parameters at the two highest concentrations, were also noticed. However, these blood component changes were within normal ranges and did not show signs of haematological toxicity and were considered of minimal toxicological importance. Noticeable histopathological changes associated with the kidney weight increases were an increase in incidence of kidney lesions in male rats at the two highest concentrations. These renal effects may not be relevant to human toxicity because these lesions were closely related to male specific nephropathy in this animal species.

Based on the lowest concentration in which there is significant increase in weight in the adrenals of both male and female rats, and in the kidneys of female rats, the US EPA (1998) considers 1,202 ppm (5,909 mg/m³) as a lowest-observed-adverse-effect level (LOAEL). The no observed adverse effect level (NOAEL) was detected at 496 ppm (2,438 mg/m³).

In a 13-week rat inhalation study performed by Union Carbide (see Section 11.4), rats were exposed for six hours per day five days a week to concentrations of isopropyl benzene between 0 and 5,900,000 µg/m³, with no mortality. Exposure to this compound did not show a significant difference in motor activity, auditory function, and body weight between exposed and non-exposed rats. In the higher exposure group, a significant increase in the weight of the liver, lung and adrenal glands was found for females. However, in male rats, only an increase in the liver weight was noted.

In a 4-week inhalation study performed by Monsanto (1986), rats showed a LOAEL of 517,000 µg/m³ (105 ppm) for central nervous system effects (i.e. side-to-side head movements and head-tilt) as well as nasal irritation. Increases in kidney weights were also observed in male and female rats. However, this neurotoxicity was not observed in other studies, such as Cushman *et. al.* (1995), described by the US EPA (1998).

3.3 Developmental and Reproductive Toxicity

Sprague-Dawley rats exposed to 0, 99, 488 or 1,211 ppm (0, 487, 2,399, or 5,953 mg/m³) of isopropyl benzene for 6 hours/day on gestation days 6-15 did not show any developmental effects at the highest dose tested. At this dose there was significant decrease in body weight in the dams, a slight increase in relative liver weight. The US EPA (1998) identified a maternal NOAEL of 488 ppm or 2,399 mg/m³ and a developmental NOAEL of 1,211 ppm (5,953 mg/m³).

In another study, rabbits exposed to isopropyl benzene at 0, 492, 1206, or 2,297 ppm (0, 2,418, 5,928, or 11,292 mg/m³) for 6 hours/day on days 6-18 of gestation induced both maternal and

developmental effects. A NOAEL of 1,206 ppm (5,928 mg/m³) was observed (Bushy Run Research Centre, 1989 as cited in US EPA, 1998).

3.4 Genotoxicity

Isopropyl benzene has been tested in various mutagenicity assays. Results in a reverse mutation assay in *S. Typhimurium* (modified Ames assay), an Ames assay, a set of HGPRT (hypoxanthine-guanine-phosphoribosyl transferase) assays and a *in vivo* micronucleus assay (in mice) were negative. The result of a micronucleus assay in rats showed a weak positive, but there was no clear dose response relationship. Equivocal results were found in cell transformation tests using BALB/3T3 cells (US EPA, 1998)

3.5 Carcinogenicity

The carcinogenicity potential of isopropyl benzene cannot be determined because of the lack of epidemiological, occupational or long-term *in vivo* animal data. Information based on the metabolic pathways of isopropyl benzene and on the structural-activity relationship study do not appear to support a carcinogenic role for this compound (US EPA, 1998).

3.6 Environmental Effects

There are very limited data for effects on terrestrial wildlife caused by isopropyl benzene. An oral LD₅₀ for isopropyl benzene in the blackbird, *Agelaius phoeniceus*, was found to be 98 mg/kg (HSDB, 1999).

Ninety-six-hour LC₅₀ values range from 2.7 mg/l for rainbow trout, *Oncorhynchus mykiss* (Galasssi et al, 1988) to 6.32 mg/L for fathead minnow (*Pimephales promelas*) (Geiger et al, 1986), indicating that isopropyl benzene is moderately toxic to fish species. The water flea, *Daphnia magna*, may be somewhat more sensitive to isopropyl benzene than fish species as 48-hour LC₅₀ values for the water flea range from 0.6 mg/L (HSDB, 1999) to 4.0 mg/L (Glickman et al, 1995).

4.0 Existing Air Quality Criteria

4.1 Overview

Currently, there is a half-hour POI guideline of 100 µg/m³ as well as an 1-hour AAQC of 100 µg/m³ (MOEE, 1994a). There is no 24-hour AAQC established for isopropyl benzene.

In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency specific summaries of information guidelines for isopropyl benzene are presented in Section 11.0 of this report. A brief summary is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE normally uses a factor of 15 to convert from criteria based on annual average concentrations, and a factor of 3 to convert from criteria, based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of all the agencies reviewed, only four had developed air criteria for isopropyl benzene: The US EPA, Michigan, New Jersey and New York. The RfC of 400 $\mu\text{g}/\text{m}^3$ from the US EPA is a re-evaluated value, based on a recent toxicological report. The Michigan 24-hour Initial Threshold Screening Level (ITSL) of 87 $\mu\text{g}/\text{m}^3$ was derived from a rat inhalation study using the EPA method for RfC development. The New-Jersey annual maximum guideline of 9 $\mu\text{g}/\text{m}^3$ is derived from the previous RfC of the US EPA, based on an evaluation of another rat inhalation study as found in HEAST (1993). These two guidelines differ mainly in the uncertainty factor used to derive them.

New York is currently in the process of setting guidelines based on the occupational limits (Threshold Limit Value - Time Weighted Average, TLV-TWA) of the American Conference of American Industrial Hygienists (ACGIH). Workplace exposure limit for isopropyl benzene set by OSHA (1989) and ACGIH (1991) is a PEL (permissible exposure limit) of 246 mg/m^3 (50 ppm) averaged over an eight-hour working period. These occupational exposure limits denote a limit for the effect of isopropyl benzene through skin absorption.

4.2 Evaluation of Existing Criteria

The US EPA has re-assessed its inhalation RfC for isopropyl benzene based on a recent animal study. The updated RfC of 400 $\mu\text{g}/\text{m}^3$ is based on the effects of this compound on kidney and adrenal weight increases in an inhalation exposure study in Fisher 344 rats (Cushman *et. al.*, 1995 as cited in US EPA, 1998). The lowest-observed-adverse-effect level (LOAEL) of 1,202

Table 1. Summary of Existing Air Quality Guidelines^a for Isopropyl benzene

Agency	Guideline Value ^b	Basis of Guideline	Date ^c	Comments
US EPA (IRIS)	400 µg/m ³ (daily for a lifetime)	RfC, toxicological evaluation - increased kidney and adrenal weights	1998	Recently developed Inhalation RfC based on toxicological assessment
California	none			No value found
Massachusetts	none			No value found
Michigan (DEQ)	87 µg/m ³ (24-hour average ITSL)	RfC, toxicological evaluation - liver, kidney, adrenal gland weights; Michigan Air Quality Division data evaluation	1994	NOAEL of 487,000 µg/m ³ from a 13-week rat inhalation study by Union Carbide (1991) - used to calculate the RfC
New Jersey	9 µg/m ³ (maximum annual average ambient air concentrations)	RfC; from HEAST (US EPA, 1993) central nervous system effects; nasal irritation	1994	LOAEL of 517,000 µg/m ³ from a 1986 4-week rat inhalation study by Monsanto - used to calculate the RfC
New York	none			In the process of development
WHO	none			No value found
Netherlands	none			No value found
Sweden	none			No value found
Canada (CEPA)	none			Not in PSL-1 or PSL-2
Ontario	100 µg/m ³ (half-hour POI guideline); 100 µg/m ³ (1-hour AAQC)	Both criteria are based on the odour effect	1979	POI guideline

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- The typical air concentration conversion factor is 1 ppm = 4,920 µg/m³ at 25°C (US EPA, 1997). Ontario uses a conversion factor of 1 ppm = 5,180 µg/m³ to reflect a typical Ontario annual average ambient temperature of 10°C (Ambient Air Quality Criteria, Regulation 337 under the Environmental Protection Act, Ontario Regulation 872/74). However, the former conversion factor has been used whenever conversion was necessary to compare data expressed in µg/m³ in this report.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

ppm (5,909 mg/m³) was determined based on significant weight increases in the adrenals of both male and female rats and in the kidneys of female rats. The next lower dose of 496 ppm (2,438 mg/m³) was considered a no-observed-adverse-effect level (NOAEL). Renal lesions observed in male rats at 496 ppm were discounted, as these are considered responses that are specific to male rats and are of no relevance to human responses.

Using the NOAEL of 496 ppm (2,438 mg/m³), the US EPA has derived an inhalation RfC of 400 µg/m³ (see Section 11.1). The NOAEL was adjusted for continuous exposure and uncertainty factors of 10 for human variability, another factor of 10 for extrapolation from a subchronic to chronic exposure, 10^{1/2} for extrapolation from animals to humans, and 10^{1/2} for lack of a multigenerational reproductive study. The US EPA also conducted a benchmark analysis on the data of the study of Cushman *et. al.* (1995). Based on the weight gain data of the male adrenal glands, a BMC₁₀ (the lower 95% confidence bound on the concentration of the maximum likelihood estimate of a 10% relative weight change) was found to be 484 ppm (2,372 mg/m³), almost the same as the NOAEL of 496 ppm (2,438 mg/m³). Modelling for the benchmark dose with the data of female adrenal weight and female kidney weight increases were not successful because a discontinuity in dose-response had occurred.

US EPA (1998) indicates an overall confidence in the RfC for isopropyl benzene as medium. The critical study used was well conducted in experimental design, however, only subchronic duration was employed. Acceptable developmental studies were carried out in rats and rabbits, however multi-generational reproductive and 2-year chronic studies are not available

The reference concentration (RfC) used by the State of Michigan to derive its Initial Threshold Screening Level (ITSL) is based on the NOAEL value of 487,000 µg/m³ obtained from a 13-week rat inhalation study performed by Union Carbide (see Section 11.4). In this study, rats were exposed for six hours per day and five days a week to concentrations of isopropyl benzene between zero and 5,900,000 µg/m³, with no mortality. Exposure to this compound did not show a significant difference in motor activity, auditory function, and body weight between exposed and non-exposed rats. In the higher exposure group, a significant increase in the weight of the liver, lung and adrenal glands was found for females. However, in male rats, only an increase in the liver weight was noted. The RfC of 87 µg/m³ was derived using the method described for RfC development by the US EPA (uncertainty factors totaled 1,000 and adjusted for 24-hour exposures with a factor of 5.6).

New Jersey has derived a RfC of 9 µg/m³ for its annual ambient air concentration guideline based on the RfC reported in HEAST (US EPA, 1993). The RfC was derived from data based on a 4-week rat inhalation study (Monsanto, 1986) where the rats showed central nervous system effects (i.e. side-to-side head movements and head-tilt) as well as nasal irritation. The resulting LOAEL of 517,000 µg/m³ (105 ppm) was then converted to a chronic RfC and this was used as the maximum annual average

concentration. The uncertainty factor used to calculate the RfC, which was then used by New Jersey, is ten times larger than the one used by Michigan (Held, 1997). However, this neurotoxicity was not observed in studies such as Cushman *et. al.* (1995) described by the US EPA (1998). It should be noted that the Monsanto study (1986) also showed increases in kidney weights in male and female rats.

New York has no current guideline for isopropyl benzene. However, proposals of short-term and annual guideline concentrations, 59,000 $\mu\text{g}/\text{m}^3$ and 585 $\mu\text{g}/\text{m}^3$, respectively, based on ACGIH TLV-TWAs are currently under consideration (S. deSantis, 1997).

For occupational regulations, the National Institute for Occupational Safety and Health (NIOSH, 1994) and the Occupational Safety and Health Administration (OSHA, 1989) as well as the American Industrial Hygiene Association (ACGIH, 1991) recommend a limit of 246,000 $\mu\text{g}/\text{m}^3$ for an 8-hour workday exposure (TLV-TWA), 40-hour work week. These values are based on human health effects to prevent narcosis, irritation of the eyes and upper respiratory tract. Isopropyl benzene also has a skin notation because of skin absorption exposure.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including isopropyl benzene, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding the completeness of relevant inhalation toxicological information examined by the Ministry and the rationale of the agencies the Ministry has considered appropriate for the development of air quality standards, specifically, the chronic inhalation REL and its rationale proposed by the State of California, and technical and economic impacts that may be anticipated consequent to the revision of air quality standards.

During the consultation period the Ministry received one submission from a stakeholder regarding the draft document for isopropyl benzene. A stakeholder from the automotive manufacturing industry suggested that the Ministry needed to raise its POI standard to be in line with the EPA's RfC.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development

of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for isopropyl benzene. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In some cases the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for Isopropyl benzene

The current Ontario half-hour POI guideline and the 1-hour AAQC are both set at $100 \mu\text{g}/\text{m}^3$, based on the odour nuisance property of isopropyl benzene.

The vapour of isopropyl benzene is irritating. The odour thresholds of this compound range from 39 to $6,370 \mu\text{g}/\text{m}^3$. The geometric mean of odour thresholds has been calculated to be $157 \mu\text{g}/\text{m}^3$ (0.032 ppm) and the geometric mean of the recognition levels is $231 \mu\text{g}/\text{m}^3$ (0.047 ppm) (AIHA, 1989). It would appear that the current POI guideline for isopropyl benzene should provide a sufficient margin to avoid the odour nuisance of this substance.

In the absence of human toxicity data, information from animal studies suggests that inhalation exposure to isopropyl benzene may induce adverse effects to the central nervous system, changes in the kidney, adrenal gland, and liver. Based on significant weight increases in the adrenal glands and the kidneys induced by isopropyl benzene, the US EPA has derived an inhalation RfC of $400 \mu\text{g}/\text{m}^3$, based on a NOAEL (no-observed-adverse-effect level) of 496 ppm ($2438 \text{ mg}/\text{m}^3$). The NOAEL has been adjusted from an intermittent exposure to a continuous exposure and a total uncertainty factor of 1000 (see section 11.1) applied to derive the RfC. The central nervous system effects usually develop at exposure levels above 500 ppm ($2450 \text{ mg}/\text{m}^3$). The ITSL criterion developed by Michigan can be considered similar to the RfC of the US EPA. The neurobehavioural effect, upon which New Jersey derived its criterion, was considered by the US EPA as non-reproducible observations. One consistent observation is that subchronic and chronic exposures to isopropyl benzene through inhalation result in increases in organ weight in experimental animals, particularly the liver and the kidneys. The NOAEL and LOAEL identified in the studies supporting the RfC of the US EPA, Michigan DEQ, and the State of New Jersey varied less than an order of magnitude (i.e. 487 - $2,438 \text{ mg}/\text{m}^3$). Much of the variability

of the RfC values comes from the use of different uncertainty factors applied to the NOAEL or LOAEL in the derivation of their respective RfC. The organ weight changes, as observed in the study from which the RfC of the US EPA was derived, would appear to be a consistent adverse effect from exposure to isopropyl benzene. Supported by detailed methods of analysis and criterion derivation, the RfC of the US EPA would appear to provide the most appropriate basis for the development of air quality standards for Ontario.

The current Ontario half-hour POI guideline of $100 \mu\text{g}/\text{m}^3$ and 1-hour Ambient Air Quality Criterion of $100 \mu\text{g}/\text{m}^3$ were established based on the nuisance odour of isopropyl benzene. A health effect-based 24-hour Ambient Air Quality Criterion can be developed using the RfC of $400 \mu\text{g}/\text{m}^3$ of the US EPA as the basis.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and accepted the scientific studies which support the RfC of the US EPA. After reviewing additional toxicological information, the Ministry has considered the uncertainty factors used to derive the RfC of $400 \mu\text{g}/\text{m}^3$ by the US EPA reasonable. Thus, the RfC becomes the health-based 24-hour AAQC of $400 \mu\text{g}/\text{m}^3$.

The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour average POI limits. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). Deriving a half-hour POI from the 24-hour AAQC of $400 \mu\text{g}/\text{m}^3$ will result in a criterion higher than the current POI guideline. Therefore, replacing the odour-based POI of $100 \mu\text{g}/\text{m}^3$ is not recommended. Considering the odour nuisance of isopropyl benzene as a sensitive endpoint, the odour-based 10-min AAQC is maintained.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and considering other relevant information such as the aesthetic effects (i.e., odour nuisance) of isopropyl benzene, the Ministry is proposing the following Ambient Air Quality Criteria and Point Of Impingement standard for isopropyl benzene:

- a 24-hour average AAQC of $400 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for isopropyl benzene based on the adverse health effects of this compound; and,
- an 1-hour average AAQC of $100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for isopropyl benzene based on the odour nuisance of this compound; and,

-
- a half-hour average POI standard of 100 µg/m³ (micrograms per cubic metre of air) for isopropyl benzene based on odour nuisance and adverse health effects.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - tuning
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.

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5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for isopropyl benzene can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* U.S. Environmental Protection Agency

3. *Guideline Value(s):*

Guideline values for isopropyl benzene appear in the U.S. Environmental Protection Agency (EPA) database IRIS (Integrated Risk Information System). The re-assessed inhalation RfC for isopropyl benzene is 400 $\mu\text{g}/\text{m}^3$.

4. *Application:*

IRIS contains health risk assessment information on over 300 chemicals. These assessments are obtained after a comprehensive review of chronic toxicity data for a given compound. An inhalation risk assessment for isopropyl benzene is under review.

5. *Documentation Available:*

US EPA, 1998. Integrated Risk Information System (IRIS) Database. Toxicological Review of Cumene. U.S. Environmental Protection Agency, Washington, DC.

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6. *Peer Review Process and Public Consultation:*

In its assessment, the US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based U.S. regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. *Status of Guideline:*

The US EPA has recently posted a revised inhalation RfC for isopropyl benzene (June 1997).

8. *Key Risk Assessment Considerations:*

The following is described in the "Toxicological Review of Cumene" (US EPA, 1998; see this review for references cited in the text).

Two successive subchronic inhalation toxicity studies were conducted with isopropyl benzene (cumene) vapours (>99.9% pure) on Fischer 344 rats. In the first study, groups (21/sex) were exposed to 0, 100, 496, or 1,202 ppm (0, 492, 2,438, or 5,909 mg/m³) cumene vapour for 6 hours/day, 5 days/week, for 13 weeks (doses adjusted for continuous exposure were 0, 88, 435, and 1,055 mg/m³). The second study was a repeat of the first, except that the group size was decreased to 15/sex, and an additional group (50 ppm, duration adjusted to 44 mg/m³) and a 4-week post-exposure period were added. Animals were sacrificed a few days after the last exposure in the first study and after the 4-week post-exposure period in the second study. Parameters monitored included clinical signs of toxicity; body weight; food and water consumption; haematology and serum chemistry; organ weights; and gross pathology and histopathology, including examination of all respiratory tract tissues (three sections of the lungs and four sections of the nasal turbinates). In both studies, evaluations of neurological function (functional observation battery [FOB] and motor activity) were conducted. In the first study, an FOB was performed on 10 rats/sex/group, and motor activity tests were conducted on 15 rats/sex/group. In the second study, motor activity tests only were performed on 15 rats/sex/group. The FOBs were performed prior to the exposure and on the weekends following Weeks 1, 2, 4, 9, and 13 of exposure; motor activity was determined prior to exposure and on the weekend following Weeks 4, 9, and 13 of exposure. The same animals were examined at each evaluation. Also in the first study, 6 rats/sex/group were perfusion-fixed for analysis of the nervous system tissues. Because cataracts were detected in the first study, a more thorough protocol was used in the second study. In the first study, the eyes were examined once by a single ophthalmologist during the last week of exposure. In the second study, eyes were examined independently by two ophthalmologists pre-exposure and at Weeks 4, 9, and 13, and at Week 4 post-exposure, and any cataracts detected were confirmed histopathologically. In the first study, sperm from epididymides (taken from 15 male rats/group) and the left testis from each male were evaluated for sperm count and

sperm morphology, and cross-sections of testes were examined for evaluation of the stages of spermatogenesis in an effort to judge the potential of cumene to cause reproductive toxicity. Auditory brain stem responses were measured at 4, 8, 16, and 30 kHz during Post-exposure Week 1 of the second study.

Transient, reversible cage-side observations during exposure periods included hypoactivity, blepharospasm, and a delayed or absent startle reflex at the highest concentration. Rats exposed to 496 ppm (2,438 mg/m³) were reported as being hypoactive during exposure, although no further specifics were given. An increased incidence of cataracts was observed in males at all exposure concentrations in the first study. These results were not observed in the second study, in which incidence of cataractous changes were not different from historical controls nor confirmed by more extensive histopathological analysis. In the first study, statistically significant ($p < 0.05$) exposure-related decreases in motor activity (ambulatory and total activity) were observed in male rats exposed to the two highest concentrations of cumene, but these results were not reproduced in the second study. There were no exposure-related changes in the FOBs in either study. No effects were observed in the neurohistopathological examinations. Evaluation of the auditory brain stem responses revealed no changes in the auditory function of the exposed animals, although 3/10 female rats in the highest exposure group were noted to have variability in their waveforms recorded at 4 kHz. These results were judged by the authors not to be indications of ototoxicity because of the variability of the responses. It also is noted that the ototoxicity known to occur with toluene, a structural analog of cumene, is evident only at frequencies of 8 kHz and higher. The only gross histopathology noted was periorbicular swelling, which occurred in animals at the two highest concentrations (and for which neither incidence nor severity was reported).

In the first study, both absolute and relative weights were increased significantly ($>10\%$, $p < 0.05$) in the kidneys, adrenal glands and livers of both sexes at the highest concentration. In females, mean kidney weights were increased 11% (absolute) and 16% (relative), adrenal weights 19% (absolute) and 26% (relative), and liver weights 34% (absolute) and 40% (relative). In males, mean renal weights were increased 12% (absolute) and 10% (relative), adrenal weights 20% (absolute) and 27% (relative), and liver weights 33% (absolute) and 30% (relative). These changes also were noted in the liver at the next lower concentration (500 ppm) for both females (7% absolute, 11% relative) and males (20% absolute, 17% relative). The results of the second study, with a 4-week post-exposure period, indicated limited reversibility of these alterations because significant mean weight increases still were present in female liver (13% absolute, 11% relative) and female adrenals (12% absolute, 8% relative) of the highest exposure group. Only male relative kidney weights (6%) and absolute liver weights (11%) remained increased significantly. These alterations in weight are considered toxicologically significant and adverse because such persistence indicates limited reversibility and uncertainty about the progression and fate of these alterations under chronic exposure. There were no cumene-related differences in weights of lungs, testes, ovaries, or brain at any exposure level in either study. At the end of the exposure in the

first study, water consumption was increased by as much as 40% in male rats at the two highest exposure concentrations. Alterations were noted in a number of haematological parameters, including a concentration-related increase in leukocytes (which is consistent with the study of Jenkins *et al.*, 1970) and platelets in males and females, as well as in lymphocytes in males at 496 (2,438 mg/m³) and 1,202 ppm (5,909 mg/m³), and significant ($p < 0.05$) decreases in erythrocyte parameters (erythrocyte count, haemoglobin, haematocrit, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration) in male rats at these concentrations. All of these alterations (except for the platelet count, which was increased by around 20% over controls, in males exposed to the highest concentration) were within normal ranges (Mitruka and Rawnsley, 1981), with no accompanying indications of haematological toxicity, and therefore are considered of minimal toxicological importance. Morphological evaluation of epididymal and testicular sperm showed no cumene-related differences in either count, morphology, or stages of spermatogenesis, although one high-dose rat did have diffuse testicular atrophy. The only microscopic effect associated with these organ weight changes was an increased incidence of kidney lesions in male rats at the two highest exposure concentrations. The incidence of hypertrophy and hyperplasia of proximal tubular epithelial cells and interstitial nephritis were increased significantly at 496 ppm (2,438 mg/m³) (12/15 and 13/15, respectively) and 1,202 ppm (5,905 mg/m³) (14/15 and 13/15, respectively) compared to controls (1/15 for each effect). There was also an increase in severity with dose in exposed renal tissues, including hyaline droplet formation, where dose-related increases in the incidence of moderate and marked severities were 2/15 (controls), 3/15, 14/15, and 14/14 (the three dose groups in ascending order of exposure concentration). The relevance of these renal effects to human toxicity is questionable because the lesion described relates closely to the male rat specific nephropathy. The US EPA has established scientific policy and several criteria for assignment of male specific renal nephropathy caused by chemicals that induce excessive accumulation of $\alpha_2\mu$ -globulin (US EPA, 1991a; Hard *et al.*, 1993). The renal histopathology reported in this study fulfills several of these criteria: lesions were limited to males; hyaline droplet formation (as confirmed by the Mallory-Heidenheim method) was noted and increased in severity in a dose-related manner; lesions associated with the pathologic sequence of $\alpha_2\mu$ -globulin nephropathy were noted, including tubular proteinosis (presumably from exfoliation of epithelial cells into the proximal tubular lumen) and tubular epithelial cell hyperplasia and hypertrophy (presumed to be regenerative from tubular necrosis). Although a major criterion not met in the study, positive identification of the accumulating protein in the hyaline droplets as $\alpha_2\mu$ -globulin, the pattern described strongly suggests male rat specific nephropathy. Chronic progressive nephropathy, which also occurs predominately in male rats, also is characterized by tubular hyperplasia and proteinosis (Montgomery and Seely, 1990), and this also may be contributory to these renal lesions. The weight alterations in the adrenals and female kidney are considered potentially adverse. The increased water consumption noted also may indicate potential for renal effects, although this effect was present at dose levels at which renal weights were not altered. Although the progression of these weight alterations from continued exposure cannot be ascertained from this subchronic study, data from the second (post-exposure) study indicate limited reversibility to the adrenals, at least in females. The liver weight alterations are not viewed as adverse

because increase in liver weight without accompanying pathology is a trait of common microsomal-inducing agents (Sipes and Gandolfi, 1991). Based on the lowest dose at which both relative and absolute weight alterations are statistically ($p < 0.05$) and biologically ($>10\%$) significant, 1,202 ppm (5,905 mg/m³) is a lowest-observed-adverse-effect level (LOAEL) based on weight alterations observed in the first study in the adrenal tissues of both sexes and the kidneys in females. The next lower dose, 496 ppm (2,438 mg/m³), is a no-observed-adverse-effect level (NOAEL).

In another inhalation study, Wistar rats were exposed to 2,500 mg/m³ cumene vapour for 8 hour/day, 6 days/week, for up to 180 days (dose adjusted for continuous duration was 714 mg/m³), and rabbits were exposed to 6,500 mg/m³ using the same exposure regimen (duration-adjusted concentration is 1,857 mg/m³). Clinical signs of toxicity, body weight, blood and bone marrow parameters, and histopathological effects (brain, cerebellum, heart, stomach, liver, pituitary, intestine, spinal cord, bone marrow, ovary, pancreas, parathyroid, lung, spleen, kidney, adrenals, testicle, thymus, thyroid, and bladder) were monitored. In the rat, the number of red blood cells decreased slightly, but no test for statistical significance was performed. Histological effects reported were "passive congestion" in the lungs, liver, spleen, kidney, and adrenals and the presence of haemorrhagic zones in the lung, haemosiderosis in the spleen, and lesions from epithelial nephritis "in some cases". It was not clear if these effects occurred in both species. Both of these exposure levels induced adverse effects.

In a related study, male and female Sprague-Dawley rats (10/sex/group) were exposed to cumene vapour concentrations of 0, 105, 300, or 599 ppm (0, 517, 1,475, or 2,946 mg/m³) for 6 hour/day, 3-5 days/week, for approximately 4 weeks (minimum exposure, 20 days) (Monsanto Company, 1986; see US EPA, 1998 for this and related studies). Urinalysis, haematology, and clinical biochemistry on serum (including BUN, SGOT, LDH, and total bilirubin) were performed. Animals were observed daily for signs of toxicity. Necropsy was performed on 5 rats/sex/group at the end of the exposure. No deaths occurred during the span of the experiment. Cage-side observations included hypoactivity in animals in the high-concentration group on some days during the exposure period. Signs of toxicity observed during the pre- or postexposure observations included concentration-related increases in side-to-side head movements in both males and females in all dose groups (combined total incidence during exposure of 0 (controls), and 14, 21, and 48 for the three dose groups), head tilt (total incidence in all dose groups of 0 (controls), and 5, 4, and 8 for the three dose groups), and arched back in one female in the high-dose group. Other less significant observations included dried, reddish discharge around the nose and near the eyes in nearly all dose groups and controls. Other effects observed in males include alopecia (mid-dose group during Weeks 2, 3, and 4 of exposure) and swollen conjunctiva during Week 4 in the high-dose group. Increases ($p < 0.05$) in mean absolute left and right kidney weights were observed high-dose males, as were increases in left kidney in low and mid-dose males. In high-dose females, the mean absolute weight of left kidneys was greater ($p < 0.05$) than in controls. No compound-related pathological changes were detected during gross or microscopic examination. Assuming that the renal changes among the males were associated with male rat specific

nephropathy, the cage-side observations of head tilt and head movements become the critical effects for this short-term study with a LOAEL of 105 ppm. This study confirms that renal weight changes occur in females, thereby corroborating similar effects reported in the study of Cushman *et al.* (1995). It should be noted that the effects associated with central nervous system perturbation (i.e., head movements) were not noted in several other longer term studies, including that of Cushman *et al.* (1995) where neurotoxicity was specifically assessed.

RfC derivation - The principal study selected is Cushman *et al.* (1995). The highest concentration tested, 1,202 ppm (5,905 mg/m³), is designated the LOAEL. The next lower dose, 496 ppm (2,438 mg/m³), is designated the NOAEL. Analyses for benchmark concentrations (BMCs) were performed on the absolute weight alterations in male and female adrenal and female renal weights. An overview of the benchmark dose approach for health risk assessments is given in US EPA (1995c). The only data set of the three that could be modelled to a level of statistical significance ($F < 0.01$) was male adrenal weights. The BMC₁₀ (the lower 95% confidence bound on the concentration from the maximum likelihood estimate of a 10% relative change) values obtained for these data were identical to one another for the two models, 484 ppm (2,372 mg/m³). The critical effect that was the most corroborated by the cumene database, however, was the increase in female kidney weight, which was not modelled successfully. Rather than rely on unsuccessful modelling results or on results from a possibly inappropriate endpoint, the NOAEL of 496 ppm (2,438 mg/m³) is used for all further quantitative analysis. It should be noted that the BMC₁₀ of 484 ppm (2,372 mg/m³) obtained for the only data set that was successfully modelled, male adrenal weight gain, is nearly the same as the NOAEL.

Calculation of the human equivalent concentration (HEC) from the NOAEL of 496 ppm is shown below:

- the NOAEL first is converted to milligrams per cubic metre and duration adjusted; then, assuming 25°C and 760 mm Hg,
 $\text{NOAEL (milligrams per cubic metre)} = 496 \text{ ppm} \times \text{MW}/24.45 = 2,438 \text{ mg/m}^3$;
- this converted value then is duration adjusted to continuous exposure, which equals the NOAEL(ADJ),
 $2,438 \text{ mg/m}^3 \times 6 \text{ hour/day} \times 5 \text{ days/7 days} = 435 \text{ mg/m}^3 = \text{NOAEL(ADJ)}$
- the scenario for this effect was a gas causing a systemic or extrapulmonary effect that assumed attainment of periodicity for the blood/air (b/a) cumene concentrations. Because no b/a lambda (i.e., partition coefficient) values for cumene are known for either animals or humans, a default value of one is used for this ratio, which indicates that there exist no differences between animals and humans in blood concentrations attained for the same air concentration of cumene;
- therefore, $\text{NOAEL(HEC)} = \text{NOAEL(ADJ)} \times [\text{b:a lambda(a)} / \text{b:a lambda(h)}] = 435 \text{ mg/m}^3 \times 1 = 435 \text{ mg/m}^3$.

The NOAEL(HEC) for increased kidney and adrenal weights in the Cushman *et al.* (1995) study is 435 mg/m³. Uncertainty factors are applied to account for recognized uncertainties in extrapolation from experimental conditions to the assumed human scenario (i.e., chronic exposure over a lifetime). Historically, UFs are applied as values of 10 in a multiplicative fashion (Dourson and Stara, 1983). Recent EPA practice, however, also includes use of a partial UF of 10^{1/2} (3.162; US EPA, 1994b) on the assumption that the actual values for the UFs are lognormally distributed. Application of these factors in the assessments is that, when a single partial UF is applied, the factor is rounded to 3, such that the total factor for a UF of 3 and 10, for example, would be 30 (3 × 10). When two partial UFs are evoked, however, they are not rounded, such that a UF of 3, 3, and 10 would result in a total uncertainty of 100 (actually 10^{1/2} × 10^{1/2} × 10¹).

The UFs applied and the justification for their use are as follows. A factor of 10 is used for extrapolation of intraspecies differences in response (human variability) as a means of protecting potentially sensitive human subpopulations. A factor of 10 is applied for subchronic to chronic extrapolation as the progression or fate of observed effects in kidney and adrenals resultant from true chronic administration is uncertain. A partial (10^{1/2}) UF is applied for consideration of interspecies extrapolation, which already has been addressed partially through the calculation of an HEC. A partial UF also is used for database deficiencies, principally because of the lack of a full-scale multi-generation reproductive study. The total UF = 10 × 10 × 10^{1/2} × 10^{1/2} = 1,000.

No modification factor (MF) is proposed for this assessment.

$$RfC = 435 \text{ mg/m}^3 \div 1,000 = 4E-1 \text{ mg/m}^3.$$

The daily exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime (the RfC) is 4E-1 mg/m³. This concentration is 1/1000 of the adjusted no-effect level for significant increases (>10%) in renal and adrenal weights in rats exposed to cumene in the subchronic inhalation study of Cushman *et al.* (1995). The overall confidence in the RfC assessment is medium. The RfC is based on rat subchronic inhalation studies performed with relatively large group sizes in which thorough histopathological analyses and ancillary studies of neurotoxicity and ocular pathology were performed. The scientific quality of this evidence is high. The confidence in the database for the cumene RfC is rated as medium. Acceptable developmental studies were carried out (via inhalation route) in two species, rats and rabbits, with no adverse results noted; however, no 2-year chronic studies are available. Full-scale multi-generation reproductive studies are lacking. The critical effect, altered tissue weights, is consistent across routes of exposure (altered kidney weight was also a critical effect for the RfD). The use of a partial uncertainty factor for interspecies extrapolation is justified because species-to-species dosimetric adjustments were made and an HEC was calculated. An area of scientific uncertainty and controversy in this assessment concerns the renal lesions in the

male rats observed in the principal study. The descriptions of these lesions strongly suggest the male-specific rat nephropathic response elicited by compounds such as *d*-limonene and decalin (US EPA, 1991a). This assessment has discounted these histopathological lesions in establishing an effect level for derivation of the RfC because US EPA does not consider such lesions to be an appropriate endpoint for determining non-cancer toxicity. If the male rat renal effects had not been discounted, then the RfD would have been approximately fivefold lower, because the NOAEL would be 100 ppm (490 mg/m³) versus 496 ppm (2,438 mg/m³). What has been accepted as toxicologically relevant from the profile of renal toxicity in the principal study is the increase in female renal weight. Other repeated-dose studies with cumene also have reported increased renal weights among female rats (Wolf *et. al.*, 1956; Monsanto, 1986; Chemical Manufacturer's Association, 1989). These independent observations, coupled with the uncertainty about the progression and outcomes of these alterations (because of the absence of any true lifetime studies) further justifies considering these weight alterations as toxicologically significant.

9. *Key Risk Management Considerations*: None, since no guidelines for ambient air exist.

10. *Multimedia Considerations of Guidelines*: None are reported.

11. *Other Relevant Factors*: None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

There are no reference levels for isopropyl benzene in the CAPCOA "Hot Spots" report and isopropyl benzene is listed under the substances for which emissions must be quantified.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results have to be prioritized. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility with another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and resubmission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. Therefore, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

Key reference(s):

CAPCOA, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines. Report of the Risk Assessment Advisory Committee, 179 pp. + Appendices.

6. *Peer Review Process and Public Consultation:*

Cancer potency slope factors, and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data for hundreds of compounds other than isopropyl benzene. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment

process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further input is expected as the process moves forward.

7. Status of Guideline:

There is no information on isopropyl benzene.

8. Key Risk Assessment Considerations:

CAPCOA "Hot Spots" information does not include information for isopropyl benzene in ambient air.

9. Key Risk Management Considerations:

The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in screening risk assessment to determine the maximum off-site cancer risk for exposed human populations. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control of volatile organic compounds, which include isopropyl benzene. It appears that the options are under local control and are based on local risk, socio-economic analyses and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (DEP)

3. *Guideline Value(s):*

There are no Allowable Ambient Limits (AAL) or Threshold Exposure Limits (TEL) for isopropyl benzene specified by the Massachusetts Department of Environmental Protection (DEP). The chemicals selected by the DEP were chosen as a representative sample to develop and test the proposed evaluation system. Health assessment of new chemicals is made on a case-by-case basis using the standardized approach developed by the DEP.

4. *Application:*

The guidelines are to be used mostly to assist in awarding permits, to verify compliance and enforcement and to be used as reference for regulatory actions. The guidelines consider the protection of public health and welfare irrespective of technological, economic and enforcement limitations.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Key Reference(s):

Office of Research and Standards (ORS), 1994. Letter from the ORS to the DEP, October 1994, 10 pp.

- 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations,
- 2) Publication of updated list of Massachusetts AALs and TELs,
- 3) Incorporation of inhalation reference concentrations into the CHEM/AAL process and,
- 4) Decisions made by ORS regarding some discrepancies observed in the RfC methodology.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) Values and Annual Average Allowable Ambient Limit (AAL) Values.

6. Peer Review Process and Public Consultation:

The guidelines are not systematically peer-reviewed but are updated and modified by the DEP at a rate of 25 to 40 AALs per year and when revision is warranted. However, public consultation is solicited in public meetings and peer-reviews are organized.

7. Status of Guideline:

Isopropyl benzene is not on the list of chemicals to be evaluated.

8. Key Risk Assessment Considerations:

The Massachusetts system uses hazard assessment only and does not use the number of exposed individuals as a criterion for regulatory action except for prioritizing regulatory activities.

9. Key Risk Management Considerations:

The Department of Environmental Protection believes that the evaluation system of AALs can minimize risks effectively while maintaining a practical regulatory approach to air Toxics.

10. Multimedia Considerations of Guidelines:

The Massachusetts' guidelines cover only ambient air but include a contribution factor of 20% in the establishment of Threshold Effect Exposure Limits (TEL). This factor assumes that 20% of the exposure is due to air for any given compound.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* Michigan State, Department of Environmental Quality

3. *Guideline Value(s):*

Michigan's 24-hour Initial Threshold Screening Level (ITSL) is equal to the RfC of 87 $\mu\text{g}/\text{m}^3$ and is based on a non-carcinogenic end-point.

4. *Application:*

The guidelines are developed by the Toxics Unit of the Michigan Department of Natural Resources for implementation of the Michigan's air toxic rules no. 230 and 232. The rules apply to new and modified processes which emits toxic air contaminants and for which an application for a permit is required and.

5. *Documentation Available:*

Michigan Department of Natural Resources, 1995/1997. Air Toxics Screening levels. Air Quality Division. 6 pp. + Appendices.

Key Reference(s):

NIOSH, 1992. NIOSH Recommendations for Occupational Safety and Health: Compendium of Policy Documents and Statements. Cincinnati, OH: National Institute for Occupational Safety and Health. DHOWS. NIOSH publication no. 92-100.

Union Carbide, 1991. Cumene (Isopropyl Benzene): Thirteen-Week Vapour Inhalation Study in Rats. TSCATS/406564, EPA/OTS; Doc # 86-910001018, NTIS/OTS0532654.

EPA, 1990. Interim Methods for Development of Inhalation Reference Concentrations - Review Draft. EPA/600/8-90/066A.

6. *Peer Review Process and Public Consultation:*

The guidelines are reviewed by the Toxics Unit upon requests for permits for certain compounds and information is based on the latest literature review.

7. *Status of Guideline:*

Current and updated information according to Air Toxics unit.

8. *Key Risk Assessment Considerations:*

The 24-hour ITSL value for isopropyl benzene was provided by the Michigan Department of Environmental Quality and is based on the NOAEL value of $487,000 \mu\text{g}/\text{m}^3$ obtained from a 13-week vapour inhalation study on Fischer 344 rats by Union Carbide (1991). In this study, rats were exposed for six hours per day and five days a week for 13 weeks to isopropyl benzene concentrations ranging between zero and $5,900,000 \mu\text{g}/\text{m}^3$, with no mortality. Exposure did not cause significant changes in motor activity, auditory functions and body weight between exposed and non-exposed rats. Liver weights in males increased at higher exposure levels. A significant increase in liver, lung and adrenal glands was found for females in the higher exposure group. The final RfC of $87 \mu\text{g}/\text{m}^3$ was obtained based on interim EPA methods for development of inhalation reference concentrations, and the application of uncertainty factors of 10 for extrapolation from animal to human, 10 for sensitive individuals, and 10 for sub-chronic to chronic extrapolation. The value was also adjusted for a 24 hour averaging time (factor of $168/30 = 5.6$). The global factor by which the NOAEL value was divided is, therefore, 5,600.

9. Key Risk Management Considerations:

Risk assessment considers that for each source, the best available control technology should be used.

10. Multimedia Considerations of Guidelines:

Information is available for ambient air only.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* New Jersey Department of Environmental Protection

3. *Guideline Value(s):*

The reference concentration for inhalation (RfC) is $9 \mu\text{g}/\text{m}^3$ for isopropyl benzene in the New Jersey Department of Environmental Protection (NJDEP) air quality permitting program. This value is based on long-term (maximum annual average) ambient air concentrations.

4. *Application:*

The list of reference concentrations for inhalation are maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consists of two levels. The first level risk screening uses information from permit applications and generalized worst case assumptions to estimate risk from inhalation. Sources which fail the first level screening are submitted to a second level risk screening which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources which fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation.

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

Monsanto Company, 1986. One-month study of cumene vapour administered to male and female Sprague-Dawley rats by inhalation. U.S. EPA/OTS Public Files, 8D submission. Microfiche No. OTS0513229.

US EPA, 1993. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, DC.

1990 Clean Air Act List of Hazardous Air Pollutants.

US EPA, 1993. Health Effects Assessment Summary Tables. HEAST Database, U.S. Environmental Protection Agency, Washington, DC.

6. Peer Review Process and Public Consultation:

The information is provided by the New Jersey Department of Environmental Protection and the Federal Standards, and new evaluations are conducted by the risk management committee that evaluates the application to determine whether the source's permit should be approved.

7. Status of Guideline:

Current and updated information according to the Review Committee.

8. Key Risk Assessment Considerations:

The Air Quality Program uses two approaches for risk assessment depending upon the type and size of the facility or source. These are refined risk assessment or risk screening. The risk assessment is based on the probability of adverse health effects resulting from human exposure to substances. The risk screening is performed in house for new and modified sources, batch operations and pilot plants. Isopropyl benzene is listed with air toxics for which the emitting facility or source must submit a refined risk assessment.

The maximum annual average ambient air concentration for isopropyl benzene used by New Jersey is taken from the HEAST report of the US EPA (1993) which is based on the LOAEL value of 517,000 $\mu\text{g}/\text{m}^3$ (105 ppm) obtained from a 4-week rat inhalation study by Monsanto Company (1986). In this study, rats showed involvement of the central nervous system and irritation of the nose. The final RfC of 9 $\mu\text{g}/\text{m}^3$ was calculated for chronic effects after the application of a final uncertainty factor of 10,000 and including consideration for extrathoracic gas:respiratory effect.

Male and female Sprague-Dawley rats (10/sex/group) were exposed to cumene vapour concentrations of 0, 105, 300, or 599 ppm (0, 517, 1,475, or 2,946 mg/m^3) for 6 hour/day, 3-5 days/week, for approximately 4 weeks (minimum exposure, 20 days) (Monsanto Company, 1986; see US EPA, 1998 for this and related studies). Urinalysis, haematology, and clinical biochemistry on serum (including BUN, SGOT, LDH, and total bilirubin) were performed. Animals were observed daily for signs of toxicity. Necropsy was performed on 5 rats/sex/group at the end of the exposure. No deaths occurred during the span of the experiment. Cage-side observations included hypoactivity in animals in the high-concentration group on some days during the exposure period. Signs of toxicity observed during the pre- or post-exposure observations included concentration-related increases in side-to-side head movements in both males and females in all dose groups (combined total incidence during exposure of 0 (controls), and 14, 21, and 48 for the three dose groups), head tilt (total incidence in all dose groups of 0 (controls), and 5, 4, and 8 for the three dose groups), and arched back in one female in the high-dose group. Other less significant observations included dried, reddish discharge around the nose and near the eyes in nearly all dose groups and controls. Other effects observed in males include alopecia (mid-dose group during Weeks 2, 3, and 4 of exposure) and swollen conjunctiva during Week 4 in the high-dose group. Increases ($p < 0.05$) in mean absolute left and right kidney weights

were observed high-dose males, as were increases in left kidney in low and mid-dose males. In high-dose females, the mean absolute weight of left kidneys was greater ($p < 0.05$) than in controls. No compound-related pathological changes were detected during gross or microscopic examination. Assuming that the renal changes among the males were associated with male rat specific nephropathy, the cage-side observations of head tilt and head movements become the critical effects for this short-term study with a LOAEL of 105 ppm. This study confirms that renal weight changes occur in females, thereby corroborating similar effects reported in the study of Cushman *et al.* (1995). It should be noted that the effects associated with central nervous system perturbation (i.e., head movements) were not noted in several other longer term studies, including that of Cushman *et al.* (1995) where neurotoxicity was specifically assessed.

9. Key Risk Management Considerations:

Risk management issues are referred to the Risk Management Committee of the NJ DEP. Other risk management considerations for isopropyl benzene are not discussed in the information document.

10. Multimedia Considerations of Guidelines:

Information submitted by applicants for Refined Risk Assessment is for ambient air only.

11. Other Relevant Factors:

None.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

Under section iv.A.2.c.1., for contaminants without numerical guidance, the contaminant must be limited to the value of $0.1 \mu\text{g}/\text{m}^3$ for moderate toxicity compounds, and $1.0 \mu\text{g}/\text{m}^3$ for low toxicity compounds. Isopropyl benzene has no guideline value. If isopropyl benzene were classified as a moderate toxicity compound, the recommended value would be $0.1 \mu\text{g}/\text{m}^3$.

New York is in the process of setting guidelines for isopropyl benzene based on ACGIH TLV-TWA values. The Short-term Guideline Concentration (SGC) will most probably be set at $59,000 \mu\text{g}/\text{m}^3$, calculated as the TLV/4.2, and the Annual Guideline (AGC) will probably be set at $585 \mu\text{g}/\text{m}^3$ calculated as the TLV/420 (S. deSantis, Personal communication).

4. *Application:*

"... the guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Albany, New York NY, 20 pp. + Appendices.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

The guidelines do not constitute a standard and are not peer-reviewed. The guidelines are updated by the New York Department of Environmental Conservation (NY DEC) as new toxicological data are available and when there are changes in the occupational values. New chemicals are evaluated by the NY DEC on demand by the public.

7. Status of Guideline:

Current, but isopropyl benzene is not addressed specifically.

8. Key Risk Assessment Considerations:

Chemical compounds are evaluated on the basis of low or moderate toxicity or high toxicity (carcinogens). Currently, there are no risk assessment considerations for isopropyl benzene.

9. Key Risk Management Considerations:

Risk management is performed by monitoring by the source owner or his authorized agent and during selected sampling by DEC staff. Impact screening analyses used in the permitting process include a guide and a computer model described in the NY State guide.

10. Multimedia Considerations of Guidelines:

The NY guidelines cover only ambient air.

11. Other Relevant Factors:

Most of the values are based on the occupational exposure limits existing for a given compound.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Isopropyl benzene.

2. *Agency:* World Health Organization.

3. *Guideline Value(s):*

There are no guidelines for isopropyl benzene.

4. *Application:*

No guidelines are applicable for isopropyl benzene.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No.

23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426 pp.

Key Reference(s):

WHO/Nordic Council of Ministers, 1985. Environmental Health Criteria No. 5: Organic solvents and the central nervous system. Copenhagen: WHO, 274 pp.

6. *Peer Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

No guideline.

8. *Key Risk Assessment Considerations:*

No risk assessment considerations of isopropyl benzene.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Isopropyl benzene is classified under organic substances of class go.2 for emissions in gaseous or vaporous form. For that class, the emission standard applicable is 100,000 µg/m³ (class go.2) with a mass flow of 2.0 kg/hour or more.

4. *Application:*

Emission standards by NeR standards have no legal status but are used as a basis for consultation for licensing with regard to emission sources calling for abatement measures using the best available technology. The NeR standard constitutes an upper limit for emissions. The nature of the substances determines the standards to be applied and whether the flow of emissions is treated or not. Emission standards must be compatible with air quality standards listed in appendix 1 which is not the case for isopropyl benzene.

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A Review of Environmental Quality Objectives and their Policy Framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, the Netherlands. 465 pp.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, the Netherlands. 81 pp. + Appendices.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

The emission standards are provided by NeR Staff Office in collaboration with other governmental agencies. Values are adjusted and updated annually, and as modifications are requested, and updates are published in amendments to the standards.

7. *Status of Guideline:*

Currently applicable and reviewed annually.

8. *Key Risk Assessment Considerations:*

Substances identified by NeR are those whose emissions to air exceed 1,000 kg per year according to the Dutch Registration of Emissions to Air. The main objective of the standard is to limit emissions to the air.

9. *Key Risk Management Considerations:*

Emission standards depend on the type of enterprises or plants. Emissions can be controlled using process-integrated measures, by limiting emissions (flow/concentration) or using add-on technologies.

10. *Multimedia Considerations of Guidelines:*

No considerations are presented for isopropyl benzene. However, multimedia exposure was not considered in the development of the current air limits for hydrocarbons. Inter-compartmental criteria which address this problem are being developed. A specific schedule for revisions based on this process has not been announced.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

Isopropyl benzene is not addressed specifically under the guidelines from the Swedish Institute of Environmental Medicine (Victorin, 1993).

4. *Application:*

Not applicable.

5. *Documentation Available:*

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. *Chemosphere*, 27: 1691-1706.

Key Reference(s):

Victorin, K., 1997. Personal communication.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No official status, but it has been used as ad hoc basis by Swedish Regulators along with WHO guidelines.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.





11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Isopropyl benzene

2. *Agency:* Environment Canada and Health Canada

3. *Guideline Value(s):*

A revision is underway (PSL 2), however, isopropyl benzene is not on the list of substances under examination.

4. *Application:*

None.

5. *Documentation Available:*

Canadian Environmental Protection Act (CEPA), 1993-94. CEPA Priority Substance List (PSL 1).
Environment and Health Canada.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either <i>Reference Exposure Level</i> as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or <i>Recommended Exposure Limit</i> used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
METHANOL**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for the development of air standards for the next several years. Methanol was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information published since the existing standards were established. A review of scientific and technical information relevant to setting an ambient air quality standard for methanol has been provided to stakeholders for comment. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for methanol.

Methanol, CAS # 67-56-1, is a clear, colourless, very mobile liquid with a slight alcoholic odour in its pure form. The crude material may have a repulsive, pungent odour. Methanol is a raw material in the production of the gasoline additive, methyl *t*-butyl ether, as well as in the production of formaldehyde, acetic acid, chloromethanes, methyl methacrylate, methylamines, and dimethyl terephthalate. It is used as a solvent or antifreeze in paint strippers, aerosol spray paints, wall paints, carburetor cleaners, and car windshield washer fluid compounds. Methanol is also a gasoline additive and a gasoline substitute for use in certain automobiles and other small engines.

Methanol has often been reported as one of the top pollutants by release quantities in Ontario, according to the National Pollutant Release Inventory of Environment Canada. During the reporting years of 1994 to 1997, three to four of the top ten methanol emitting facilities in Canada were located in Ontario. The 1994 report indicated that 105 facilities released 3,819 tonnes (57% of total to all media) of methanol to air in Ontario. The releases increased to 4,951 tonnes as shown in the 1997 report. The highest releases in Ontario were generated from the pulp and paperboard industry. Other large emissions came from the plastic and synthetic resin industry.

Methanol is readily absorbed through inhalation, ingestion, and dermal exposures. Once absorbed, methanol is oxidized to formaldehyde and then to formic acid. Formate appears to be the metabolite responsible for most of the toxic effects of methanol. The most common symptoms of exposure are visual disturbances, including blindness as an extreme case, and metabolic acidosis. Other symptoms include dizziness, nausea, vomiting, unsteady gait, vertigo, multiple neuritis with paresthesia, pains in the extremities, and headaches.

The United States Environmental Protection Agency (US EPA) has not evaluated methanol for evidence of human carcinogenicity. No information was found on the carcinogenicity of methanol to humans or animals. The US Department of Human and Health Services is currently studying the carcinogenicity potential of methanol in animals through the National Toxicology Program.

The current Ontario half-hour Point Of Impingement standard for methanol is $84,000 \mu\text{g}/\text{m}^3$ and the 24-hour Ambient Air Quality Criterion is $28,000 \mu\text{g}/\text{m}^3$. These levels were established more than 20 years ago on the basis of health effects.

The documentation for ten agencies, including the United States Federal Government, the States of California, New York, New Jersey, Michigan and the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government, was reviewed for the existence and basis of air quality criteria for methanol.

The US EPA's Reference Concentration (RfC) for methanol is under review. The Netherlands has set an emission standard for methanol which is used in permitting. The World Health Organization, Sweden, and the Canadian Federal Government have not set air quality guidelines for methanol. The States of California, Michigan, New Jersey, New York and the Commonwealth of Massachusetts have promulgated air quality guidelines or Reference Exposure Levels (REL) for methanol based on occupational exposure limits. The California Environmental Protection Agency (California EPA) is proposing a revision of its chronic (long-term) inhalation REL based on developmental effects in mice, and an acute (short-term) inhalation REL based on central nervous system effects in humans.

Of the criteria reviewed, the Ministry has evaluated and accepted the rationale which support the development of the current chronic REL of $620 \mu\text{g}/\text{m}^3$ from the California EPA. This REL has also been adopted by the State of New Jersey as its RfC. After reviewing additional toxicological information, the Ministry has derived a 24-hour AAQC of $3,100 \mu\text{g}/\text{m}^3$ for methanol based on the rationale for California's current chronic REL.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion and Point of Impingement standard for methanol:

- **a 24-hour average AAQC of $3,100 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methanol based on the adverse health effects of this compound; and**
- **a half-hour average POI standard of $9,300 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methanol based on the adverse health effects of this compound.**

Since methanol is a commonly used substance in various industries in Ontario, immediate compliance with this proposed POI standard may be difficult for some industries. Stakeholder comments are requested regarding any technical and/or economic impacts that may be encountered as a result of the

revised POI standard. The comments received from stakeholders will help to determine whether or not risk management is required and if so, its extent.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Methanol was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information published since the existing standards were established more than 20 years ago. A review of scientific and technical information relevant to setting an ambient air quality standard for methanol has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an AAQC and a half-hour POI standard for methanol.

2.0 General Information

2.1 Physical/chemical Properties

The following list provides some general information on methanol and its properties:

CAS #	67-56-1
RTECS #	PC1400000
UN #	1230
Conversion Factors	1 ppm = 1.31 mg/m ³ @ 25 °C and 1 atm 1 mg/m ³ = 0.76 ppm @ 25 °C and 1 atm
Boiling Point	64.7 °C at 760 mm Hg
Flash Point	12 °C
Henry's Law Constant	4.55 x 10 ⁻⁶ atm m ³ /mol
Log K _{OW}	-0.77
Formula	CH ₃ OH
Molecular Weight	32.05 g/mol
Vapour Density (air = 1)	1.11
Vapour Pressure	100 mm @ 21.2 °C, 126 mm @ 25 °C
Common Synonyms	Methyl alcohol, wood alcohol

Methanol is a clear, colourless, very mobile liquid. It has a slightly alcoholic odour in a pure form, whereas the crude material may have a repulsive, pungent odour (Lewis, 1992). The odour detection thresholds range from 5.5 mg/m³ to 7794 mg/m³, with an geometric mean of 209 mg/m³ (AIHA, 1989).

2.2 Uses of Methanol

Methanol is a raw material in the production of the gasoline additive methyl *t*-butyl ether, as well as compounds such as formaldehyde, acetic acid, chloromethanes, methyl methacrylate, methylamines, and dimethyl terephthalate. It is used as a solvent or antifreeze in paint strippers, aerosol spray paints, wall paints, carburetor cleaners, and car windshield washer compounds. Methanol is also a gasoline additive and a gasoline substitute for use in certain automobiles and other small engines (US EPA, 1994).

2.3 Sources and Levels

Sources

Methanol occurs naturally in wood and in volcanic gases, and is a by-product of decaying organic matter (US EPA, 1994). It is also produced industrially. Methanol is listed on Environment Canada's National Pollutant Release Inventory (NPRI), for reporting releases of this chemical to the environment by industrial facilities (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996). Methanol accounts for nearly 8% of all pollutant releases to air in Ontario, as reported in the NPRI for 1996. In the 1994 report, 105 Ontario facilities released 3,819 tonnes (57% of total to all media) to air in Ontario. In the 1997 report, 85 sources released 4,951 tonnes of methanol to the atmosphere in Ontario. The highest emitters in Ontario were in the pulp and the paperboard industry. Methanol is formed as a by-product during the pulping process and is emitted at several points in a paper mill. Other large emissions came from the plastic and synthetic resin industry. Review of the NPRI database for 1995 revealed that some of the pulp and paper companies released 88%-95% of their methanol emissions to water, but one of the more progressive companies released 99% to air. Reported in the 1996 and 1997 NPRI databases, those same pulp and paper companies showed no significant change in their releases to air, while releases to water were reported as zero. The large decrease in the on-site releases of methanol to water was primarily due to the effluent treatment requirements of the federal pulp and paper regulations and the MISA regulations of Ontario. Releases to water are more toxic to fish and other aquatic life, while releases to air may lead to increased formaldehyde in ambient air and eventually to higher levels of ground level ozone/smog.

Ambient Air Concentrations

There was no ambient air monitoring data available for methanol either Environment Canada or the MOEE. Mean ambient concentrations of 5-35 $\mu\text{g}/\text{m}^3$ of methanol have been detected in the area of Stockholm, Sweden, and two remote Arizona locations had mean ambient concentrations of 3.4 $\mu\text{g}/\text{m}^3$ and 10.3 $\mu\text{g}/\text{m}^3$ in a 1982 study (HSDB, 1997). For several locations in the United States, the U.S. EPA has determined a mean ambient concentration of 23.1 $\mu\text{g}/\text{m}^3$ during 1990 and 1991.

A sampling of recent applications for Certificates of Approval in Ontario showed that the largest of the predicted maximum ground level concentrations (half-hour average) was approximately 21,000 $\mu\text{g}/\text{m}^3$ and the minimum was 0.0007 $\mu\text{g}/\text{m}^3$. The maximum value was attributed to ventilation from an unspecified industrial process. The mean of all GLCs in the sampling was approximately 600 $\mu\text{g}/\text{m}^3$ and the median was 25 $\mu\text{g}/\text{m}^3$. Ambient air measurements of methanol near pulp and paper mills are not available, but the predicted maximum level for one recent C of A application was only 14 $\mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

Methanol reacts with hydroxyl radicals in the atmosphere. The reaction has a half-life of 17.8 days and produces formaldehyde (US EPA, 1994). Methanol can also react with oxides of nitrogen in the presence of sunlight to form ground-level ozone, a component of smog. Biodegradation is the major route of removal of methanol from soil and water. Bioaccumulation in aquatic organisms is not expected to be significant for methanol, based on an estimated bioconcentration factor of 0.2 (US EPA, 1994).

3.0 Toxicology of Methanol

The following toxicological review of methanol focusses on inhalation, since this is considered the primary route of human exposure in Ontario. Data from the NPRI indicated that most of the methanol generated from industrial sources was emitted to the air. Data on other exposure media are included where relevant or where inhalation data are lacking.

Methanol is readily absorbed through ingestion, inhalation, and dermal routes of exposure. Following absorption, methanol is rapidly distributed to organs according to the distribution of body water. Metabolism of methanol in humans begins through oxidation in the liver by the enzyme alcohol dehydrogenase to formaldehyde, and then to formic acid. The formic acid arising from methanol oxidation by alcohol dehydrogenase and aldehyde dehydrogenase is subsequently metabolized via a folic acid-dependent pathway to carbon dioxide. Methanol is excreted as the formic acid metabolite in urine, or as the parent compound in urine or expired air (US EPA, 1994). The oxidation rate is only about one seventh of that of ethanol, so complete oxidation and excretion of methanol usually requires several days (reviewed in HSDB, 1997).

3.1 Acute Toxicity

Acute methanol intoxication by the inhalation route of exposure initially results in narcosis. In the second stage, a latent period (12-18 hours) follows during which formic acid accumulation causes metabolic acidosis. In the third stage, extreme abdominal, leg, and back pain occur and visual degradation, if sufficiently severe, can lead to blindness. One worker died from exposure to methanol vapour concentrations between 5,320 and 17,290 mg/m³ over a 12 hour period (ACGIH, 1991). The U.S. EPA estimated the exposure dose to be approximately 1,140 mg/kg in that case (US EPA, 1994). Ingestion of 80-150 mL is usually fatal and blindness may be caused by as little as 4 mL. A pilot study (Cook et al., 1991) on inhalation of methanol by humans (250 mg/m³ for 75 minutes) measured effects by means of 20 commonly used tests of sensory, behavioural and reasoning performance before, during and after exposure. Methanol had no significant effect on the subjects'

performance for all but two of the tests. Performance was slightly impaired in one test measuring memory and concentration, and brain wave patterns changed slightly in a test measuring response to light flashes and sounds. Subjects also reported higher levels of fatigue, but the changes did not affect the subjects' ability to maintain vigilance or to respond quickly to stimuli.

3.2 Subchronic/Chronic Toxicity

In humans, chronic exposure to methanol by inhalation results in headaches, insomnia, gastrointestinal problems, and blindness (US EPA, 1994). Since methanol is eliminated from the body slowly, repeated exposures result in an increased blood and tissue concentration (ACGIH, 1991). Death and blindness have frequently been the result of occupational methanol poisoning (ACGIH, 1991). Inhalation exposure to methanol concentrations between 266 and 499 mg/m³ (time period not specified) has resulted in severe and recurrent headaches in exposed workers (ACGIH, 1991; reviewed in Calabrese and Kenyon, 1991). Data from occupational health studies suggests that concentrations between 1,596 and 11,039 mg/m³ (time period not specified) are required to produce the characteristic visual disturbances, including blurred and double vision, constricted visual fields, changes in colour perception, and blindness (as cited in Calabrese and Kenyon, 1991). Clinical examination of such cases has revealed sluggish pupils, pallid optic discs, retinal edema, papilledema, and optic disc hyperaemia with blurred edges and dilated veins.

3.3 Developmental/Reproductive Toxicity

Information based on reviewed materials did not provide relevant data on the reproductive toxicity of methanol in humans (US EPA, 1994). The American Conference of Governmental Industrial Hygienists (ACGIH, 1991) described a study evaluating the teratogenic effects of inhaled methanol in rats. Pregnant rats were exposed to methanol at 0, 6650 or 13300 mg/m³ (0, 5000 and 10000 ppm) for 7 hours/day on days 1-19 of gestation. Another group of rats were similarly exposed on days 7-15 of gestation to 26200 mg/m³ (20000 ppm) methanol. These rats exhibited some maternal toxicity, such as unsteady gait. A high incidence of congenital malformations, mainly expressed as extra or rudimentary cervical ribs, and urinary or cardiovascular effects, were observed in fetuses removed on day 20 (ACGIH, 1991). Although similar malformations were seen in the 13,300 mg/m³ group, these were not significantly different from the controls. A no adverse effects level (NOAEL) was observed in the 6650 mg/m³ group (ACGIH, 1991). A more recent study has been done (Rogers et al, 1993) in which pregnant mice were exposed to methanol vapours at concentrations ranging from 1000 ppm to 15,000 ppm (1310 mg/m³ to 19650 mg/m³) for 7 hours per day, on days 6-15 of gestation. Significant increases in the incidence of exencephaly (brain formed outside skull) and cleft palate were observed at 6550 mg/m³ and higher. A dose-related increase in the number of fetuses per litter with cervical ribs (usually small ossification sites) was observed at 2620 mg/m³ and above. A NOAEL of 1310 mg/m³ was determined for the pregnant mice. In other studies, male rats exposed to 266 mg/m³

of methanol by inhalation for 6 weeks had significantly lowered testosterone levels. An additional change in luteinizing hormone was observed at 13,300 mg/m³ (US EPA, 1994).

3.4 Genotoxicity

Methanol did not induce oncogenic transformation in Syrian hamster embryo cells, *in vitro* sister chromatid exchange (cell type not specified), or aneuploidy and chromosome aberrations in *Neurospora crassa* (reviewed in Calabrese and Kenyon, 1991; US EPA, 1994). Information on the GENETOX database indicated inconclusive results in micronucleus tests and assays for chromosome aberrations in mammalian polychromatic erythrocytes (US EPA, 1994). Calabrese and Kenyon (1991) noted that methanol has been reported to; interfere with DNA repair in *E. Coli*, induce mutations in the yeast *S. cerevisiae* through direct action without metabolic activation with S9, cause chromosomal aberrations in bone marrow cells after ingestion and intraperitoneal injection in mice, and test positive in a mouse micronucleus test.

3.5 Carcinogenicity

The US EPA has not evaluated methanol for evidence of human carcinogenicity (US EPA, 1997). No information was found, based on review materials, on the carcinogenicity of methanol in humans or animals (US EPA, 1994). The National Toxicology Program in the United States is currently studying the potential for carcinogenicity of methanol. Calabrese and Kenyon (1991) also found no data implicating methanol as a carcinogen.

3.6 Environmental Effects

There are limited data for the effects of methanol exposure on terrestrial wildlife. Applications of 0.0001 to 0.6 mL methanol/kg of soil did not affect embryogenesis or oviposition in grasshoppers (*Acrotylus patruelis*) (Schmidt, 1986). Methanol has been found to have a low toxicity to aquatic organisms. A 48-hour LC₅₀ of 1,700 mg/L has been determined for goldfish (*Carassius auratus*) (US EPA, 1994). Ninety-six-hour LC₅₀ values for fish range from 20,100 mg/L for rainbow trout (*Oncorhynchus mykiss*) to 28,100 mg/L for fathead minnow (*Pimphales promelas*) (US EPA, 1994).

4.0 Existing Air Quality Criteria

4.1 Overview

Ontario currently has a 24-hour AAQC of $28,000 \mu\text{g}/\text{m}^3$ for methanol and a half-hour POI standard of $84,000 \mu\text{g}/\text{m}^3$. These criteria have been established on the basis of health effects (MOEE, 1994). As a part of the air quality criteria reviewing process for Ontario, the documentation for ten agencies, including the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government, was reviewed for the existence and basis of air quality criteria for methanol. A summary of air quality guidelines used in other jurisdictions is presented in Table 1 and reviews of specific agencies are provided in the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment typically uses a factor of 15 to convert from guidelines based on annual average concentrations, to half-hour point-of-impingement limits, and a factor of 3 to convert from guidelines based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality guidelines based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of the agencies reviewed for air quality criteria, all except The Netherlands have derived their ambient air limits for methanol from occupational exposure limits. Specifically, the criteria established by the state agencies of Michigan, Massachusetts, New Jersey and California are based on the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value-Time Weighted Average (TLV-TWA) of 200 ppm ($262 \text{ mg}/\text{m}^3$) for methanol. The New York guideline is based on the NIOSH limit of 200 ppm ($262 \text{ mg}/\text{m}^3$) (NIOSH, 1988). Depending on the state agency, a variety of uncertainty and modification factors were applied to the TLV-TWA in order to provide sufficient margin of safety when occupational exposure limits were used to derive environmental exposure criteria.

The state agency of Massachusetts considers an additional factor for multimedia exposure in their guideline derivation (MDEP, 1994). In general, the guidelines derived from the TLV range from a low of $7.13 \mu\text{g}/\text{m}^3$ (Massachusetts; 24-hour and annual average) to a high of $6200 \mu\text{g}/\text{m}^3$ (New York).

The REL of $620 \mu\text{g}/\text{m}^3$ from the state agency of California was adopted by New Jersey as their annual guideline (reference concentration for permitting). The State of California is proposing to revise its chronic reference exposure level (REL) to $10,000 \mu\text{g}/\text{m}^3$. The developmental effects of methanol were

Table 1. Summary of Existing Air Quality Guidelines^[1] for Methanol

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration): under review.		1998	No air guideline promulgated.
California	No ambient air quality criterion. REL (Reference Exposure Level): 620 $\mu\text{g}/\text{m}^3$ (annual average);	TLV-TWA from ACGIH.	1993	Methanol appears on the Toxic Air Contaminants Identification List, but has yet to undergo a needs assessment. The REL is used for permitting.
	proposed chronic REL: 10000 $\mu\text{g}/\text{m}^3$;	Developmental effects in mice	1997	
	proposed acute REL: 28000 $\mu\text{g}/\text{m}^3$ (1-hour average)	CNS effects in humans	1998	
Massachusetts	TEL (Threshold Effects Exposure Limits): 7.13 $\mu\text{g}/\text{m}^3$ (24-hour average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 7.13 $\mu\text{g}/\text{m}^3$ (annual average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
Michigan	ITSL (Initial Threshold Screening Level): 3,250 $\mu\text{g}/\text{m}^3$ (1-hour average).	TLV-STEL from ACGIH.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC (Reference Concentration for Inhalation): 620 $\mu\text{g}/\text{m}^3$ (annual average)	Chronic REL from California	1997	Adopted California's REL. Used for permitting.
New York State	AGC (Annual Guideline Concentration): 6,200 $\mu\text{g}/\text{m}^3$.	REL-TWA from NIOSH.	1992	Used for permitting.
WHO	None.			
Netherlands	150,000 $\mu\text{g}/\text{m}^3$ (half-hour average).	Emission standard.	1992	Used for permitting.
Sweden	None.			
CEPA	None.			
Ontario	POI limit: 84,000 $\mu\text{g}/\text{m}^3$ (half-hour)	Health effects.	1994	Air quality standard.
	AAQC: 28,000 $\mu\text{g}/\text{m}^3$ (24-hour).	Health effects.	1994	

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.

considered for the chronic REL. California is also proposing an acute REL of 28,000 $\mu\text{g}/\text{m}^3$, based on the subtle impairment in the performance of complicated tasks as a result of adverse effects on the central nervous system.

The Netherlands has a half-hour guideline value of 150 000 $\mu\text{g}/\text{m}^3$. No guidelines were identified for the WHO, Sweden and the Canadian federal government.

4.2 Evaluation of Existing Criteria

Most of the agencies have derived their ambient air quality criteria from the occupational exposure limits established by the ACGIH. The ACGIH recommended a TLV-TWA (8-hour average) of 200 ppm (262 mg/m^3) and a TLV-STEL (15-minute average) of 250 ppm for methanol to prevent severe recurrent headaches and diminution of vision (ACGIH, 1991). The NIOSH also recommended a REL of 200 ppm, based on similar considerations (NIOSH, 1988). The TLV-TWA is based on concentrations of airborne substances at which workers may be repeatedly exposed without adverse health effects. For these reasons, the U.S. state agencies have employed a variety of uncertainty or modification factors to the occupational exposure limits to obtain their respective air quality criteria corresponding to environmental exposures.

The differences in the values between the criteria and the guidelines determined by the various state agencies lie mainly in amplitude of the uncertainty factors employed. These factors range from a low total uncertainty factor of 42 from New York state to a high of 36,750 for the State of Massachusetts. Detailed explanations of the derivation of uncertainty factors can be found in the Appendix for the various state agencies. In short, all states include a factor of 4.2 to account for the standard 40-hour work week of discontinuous exposure to a 168-hour week for continuous environmental exposures. Other factors were also considered in order to provide sufficient margin of safety for the protection of health. Thus, New York State has classified methanol as a low toxicity chemical and considers a single factor of 10 to be adequate, resulting in a total uncertainty factor of 42.

Michigan State uses the same two factors as those of New York, but adds a third factor of 70/30 to account for a lifetime of exposure (70 years) as compared to just the working period (30 years). Michigan's total uncertainty factor is therefore 100 ($4.2 \times 10 \times 70/30 = 98$, rounded to 100), and is applied to the TLV-STEL of 325 mg/m^3 (approximately 250 ppm).

Massachusetts has applied a total uncertainty factor of 3675 to derive its guideline from the occupational exposure limit of the ACGIH. A factor of 5 has been included to account for exposure routes other than inhalation.

The California Environmental Protection Agency (California EPA) also uses the same two factors as those of the New York State, but adds a third factor of 10, because adverse health effects are often reported at the TLV-TWA level. This results in total uncertainty factor of 420 ($4.2 \times 10 \times 10$).

Health assessment of methanol for humans based on animal data has been difficult, based on studies reviewed in the ACGIH documentation (ACGIH, 1991). Some of the human toxic effects, such as metabolic acidosis and retinal degeneration, are not seen in non-primate laboratory studies. Minimum lethal concentrations and signs of intoxication vary widely with animal species. Only several species of the monkey can serve as appropriate models of the human intoxication syndrome.

In a chronic inhalation study in which rats and cynomolgus monkeys were exposed to methanol for the investigation of its toxic effects on body weight, organ weight, tissue and eyes (Andrews et al., 1987 as cited on OEHHA, 1997). No adverse effects were seen in either the monkeys or the rats after exposure to 680 mg/m^3 (520 ppm) to 6650 mg/m^3 (5010 ppm) methanol for 6 hours/day, 5 days/week, for 4 weeks. Possible neurologic or reproductive effects which have been observed in other species at lower concentrations were not examined.

A lack of toxicity data led the U.S. EPA (US EPA, 1986 as cited in US EPA, 1997) to sponsor a subchronic toxicity study on rats. Elevated levels of two liver enzymes and decreased brain weights led to the establishment of a NOAEL of 500 mg/kg/day (rats, gavage) for methanol. A total uncertainty factor of 1000 was applied to the NOAEL to establish the RfD level of 0.5 mg/kg/day .

Information on the reproductive or developmental effects in humans is limited. Some animal inhalation studies indicated that birth defects could be observed in the offspring if parents were exposed to methanol during gestation. For example, rats were exposed to 6550, 13100 or 26200 mg/m^3 methanol for 7 hours daily during their entire gestation. Significant increases in fetal defects of the skeletal, cardiac and urinary systems occurred at the highest level (as cited in ACGIH, 1991). A NOAEL of 6550 mg/m^3 was determined.

Recently the California EPA has proposed to revise its chronic REL and develop an acute REL based on recently available studies. The proposed chronic REL is based on a more recent study (Rogers et al, 1993 as cited in OEHHA, 1997) in which pregnant mice were exposed to methanol vapours at concentrations ranging from 1000 ppm to 15,000 ppm (1310 mg/m^3 to 19650 mg/m^3) for 7 hours per day on days 6-15 of gestation. Significant increases in the incidence of exencephaly (brain formed outside skull) and cleft palate were observed at 6550 mg/m^3 and other higher concentrations. A dose-related increase in the number of fetuses per litter with cervical ribs (usually small ossification sites) was observed at 2620 mg/m^3 and above. A NOAEL of 1310 mg/m^3 (1000 ppm) was determined for the pregnant mice. After applying a conversion factor for a human equivalent concentration and a total uncertainty factor of 30, a revised chronic inhalation reference exposure level of 10 mg/m^3 has been proposed. The OEHHA also calculated a maximum likelihood estimate (MLE_{05} ; using a log-logistic

model for 5% added risk above background) of 1079 mg/m³ (824 ppm), and a benchmark concentration (BMC₀₅) of 400 mg/m³ (305 ppm). The observation of a NOAEL and the demonstration of a dose-response relationship are major strengths of the proposed REL. Major weaknesses are the lack of human data for chronic inhalation exposure, the lack of long-term multiple dose studies, and the difficulty in addressing reproductive short-term effects within the chronic REL framework used by the California OEHHA.

The proposed acute inhalation REL of 28 mg/m³ of California is based on the human study of Cook *et al.* (1991 as cited in OEHHA, 1998). In this study mild adverse effects on 12 young male volunteers were measured after exposure to methanol vapours at 250 mg/m³ for a 75 minute period. This pilot study, sponsored by the Health Effects Institute, was designed to simulate potentially worst-case exposure from normal use of methanol-fuelled vehicles. The subjects were administered a battery of 20 commonly used tests of sensory, behavioural and reasoning performance before, during and after exposure. Methanol had no significant effect on the subjects' performance for all but two of the tests. Performance was slightly impaired in one test measuring memory and concentration, and brain wave patterns changed slightly in a test measuring response to light flashes and sounds. Subjects also reported higher levels of fatigue, but the changes did not affect the subjects' ability to maintain vigilance or to respond quickly to stimuli. Strengths of the proposed acute toxicity REL are the human (inhalation) data and the determination of a NOAEL (250 mg/m³ or 192 ppm). An uncertainty factor of 10 was used to account for intraspecies sensitivity. The acute REL is calculated to be 28000 µg/m³ (21 ppm). The only exposure concentration tested was considered a free-standing NOAEL for subtle neurologic effects. Major weaknesses are due to the inherent small sample size of a pilot study and the use of a single dosage level and therefore, a LOAEL could not be obtained. The California EPA will likely reevaluate their proposed acute toxicity REL when a study of the neurobehavioural effects of methanol using a larger sample size becomes available.

The Netherlands has set an emission standard for methanol which is used in permitting. None of the World Health Organization, Sweden, or the Canadian Federal Government have air quality guidelines for methanol.

5.0 Status of Stakeholder Consultation

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including methanol, for air quality standards development under the Standards Plan (MOEE, 1996). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agency guidelines of which the Ministry has considered appropriate for the development of air quality standards, particularly the rationale for the chronic and acute REL of the California EPA; and technical and economic impacts that may be anticipated consequent to the revision of the air quality standards.

During the consultation period the Ministry received two submissions from stakeholders regarding the draft document for methanol. Comments from stakeholders in the automotive manufacturing industry supported the rationale underlying the acute and chronic REL of the California EPA as a basis for the derivation of Ontario's air quality standards. The petroleum products stakeholders indicated that a minor revision in the air quality standard for methanol will not have a significant impact on their operations

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard, which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for methanol. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for Methanol

The current Ontario 24-hour AAQC for methanol is $28,000 \mu\text{g}/\text{m}^3$ and the half-hour POI standard is $84,000 \mu\text{g}/\text{m}^3$. The limiting effects for these values are health concerns.

Inhalation exposure to methanol is toxic to the central nervous system, causing nausea, dizziness, headache and damage to the visual tissues. Short-term exposure induces progressive tissue damage starting from narcosis, followed by physiological changes (acidosis) in the body with resulting pain and visual impairment, which may lead to blindness in severe cases. Death has been reported as a result of inhaling methanol vapour at concentrations between $5,320$ and $17,290 \text{ mg}/\text{m}^3$ (estimated to be an equivalent dose of $1,140 \text{ mg}/\text{kg}$) over a 12-hour period. Volunteers exposed to $250 \text{ mg}/\text{m}^3$ of methanol for 75 minutes reported increased levels of fatigue, decreased ability to concentrate and less

vigour. However, neurobehavioural and neurophysiological tests did not show significant changes. Based on these findings, the California EPA has proposed an acute (1-hour average) reference exposure level of $28,000 \mu\text{g}/\text{m}^3$. Long-term exposures to methanol induce toxic effects similar to those observed with short-term exposures such as headaches, sleep disturbances, gastrointestinal problems and blindness.

In animals, except non-human primates, the major effect of methanol intoxication is central nervous system depression. Visual impairment is not observed. Inhalation of methanol during pregnancy of animals may induce abnormalities in their fetuses. In rats and mice, exposure to methanol during gestation periods resulted in a decrease in fetal weight, an increase in extra or rudimentary cervical ribs, urinary or cardiovascular defects, development of the brain outside the skull and cleft palates. The no-observed-adverse-effect level (NOAEL) levels have been identified as $5,000 \text{ ppm}$ ($6,650 \text{ mg}/\text{m}^3$) and $1,000 \text{ ppm}$ ($1,310 \text{ mg}/\text{m}^3$) for rats and mice, respectively. Based on these observations, the California EPA has proposed a revision to its existing chronic reference exposure level from $620 \mu\text{g}/\text{m}^3$ to $10,000 \mu\text{g}/\text{m}^3$. Reproductive and developmental effects of methanol have not been reported in humans. The current chronic REL of $620 \mu\text{g}/\text{m}^3$ is derived from the TLV-TWA of the ACGIH, based on human and animal data.

Other states have also derived their guidelines based on occupational exposure limits using standard modification factors.

The odour thresholds for methanol range from $5.5 \text{ mg}/\text{m}^3$ to $7,794 \text{ mg}/\text{m}^3$ and the geometric mean value is $209 \text{ mg}/\text{m}^3$. Considering the lower threshold for the adverse health effect of methanol, odour is not an appropriate basis for air quality standards derivation.

There are insufficient data to establish an air criterion based on effects on plants. However, the proposed health-based criteria should provide sufficient protection for plants or other terrestrial organisms.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and accepted the rationale which support the development of the current chronic REL of $620 \mu\text{g}/\text{m}^3$ from the California EPA. This REL has also been adopted by the State of New Jersey as its RfC. After reviewing additional toxicological information, the Ministry has decided to derive a 24-hour AAQC of $3,100 \mu\text{g}/\text{m}^3$ for methanol based on the rationale for California's current chronic REL. The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour averaging concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure

that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion and Point of Impingement standard for methanol:

- a 24-hour average AAQC of 3,100 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methanol based on the adverse health effects of this compound; and
- a half-hour average POI standard of 9,300 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methanol based on the adverse health effects of this compound.

Since methanol is a commonly used substance in various industries in Ontario, immediate compliance with this proposed POI standard may be difficult for some industries. Stakeholder comments are requested regarding any technical and/or economic impacts that may be encountered as a result of the revised POI standard. The comments received from stakeholders will help to determine whether or not risk management is required and if so, its extent.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;

-
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
 4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the

federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for methanol can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Methanol (CAS# 67-56-1)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

A chronic inhalation Reference Concentration (RfC) for methanol is under review by an Agency work group. Methanol has not been evaluated by the US EPA for evidence of its human carcinogenic potential. No ambient air concentration guidelines exist for methanol.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

No information available.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

The US EPA, through their association with the Health Effects Institute, has sponsored recently concluded, but not yet published, studies by Thomas Burbacher (U. Washington) on the methanol metabolism and reproductive toxicity in non-human primates, and on the effects of *in utero* methanol exposure on the physical growth and behavioural development of non-human primates. The data is not yet available.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Methanol (CAS # 67-56-1)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for methanol. However, a Reference Exposure Level (REL) of $620 \mu\text{g}/\text{m}^3$ has been established for methanol, based on a threshold limit value (TLV) set by the American Conference of Governmental Industrial Hygienists (ACGIH). The OEHHA of the California EPA has proposed a chronic REL of $10000 \mu\text{g}/\text{m}^3$ and an acute REL of $28000 \mu\text{g}/\text{m}^3$ for methanol.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

The draft document on the Determination of Acute Toxicity Exposure Levels for Airborne Toxicants was released for public comment in 1996 (ARB, 1997). This report provides the supporting documentation rationale for the development of new acute toxicity exposure levels to be applied to

various airborne toxicants. It identifies key studies, summarises the human and animal health effects of these toxicants and presents the derivation of revised acute one hour RELs which will be adopted in the future. It must be noted that this is a draft document which is still undergoing public review (OEHHA, 1995).

5. Documentation Available:

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 625-627.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

Office of Environmental Health Hazard Assessment, 1995. Technical Support Document for the Determination of Acute Toxicity Exposure Levels for Airborne Toxicants.

Key Reference(s):

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OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, USA.

OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

6. Peer-Review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification List is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (e.g., Hazardous Substances Database, Integrated Risk Information System, International Agency for Research on Cancer, etc.) and additional widely recognised reference texts.

The reference concentrations (RfCs), RELs, and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines is subjected to review by the local district and the OEHHA. In addition, public input plays a

key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

The Determination of Acute Toxicity Exposure Levels for Airborne Toxicants has been released for public comment, and is currently undergoing public review.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The REL of $620 \mu\text{g}/\text{m}^3$ is based on the ACGIH TLV-Time-Weighted-Average (TLV-TWA) of $262,000 \mu\text{g}/\text{m}^3$ divided by an uncertainty factor of 420. This factor was derived by multiplying a factor of 4.2 (used to account for the extrapolation from a 40 hour work week to a 168 full week), by 10 times (to extrapolate from healthy to sensitive workers), and by another 10 times (since adverse health effects are often reported at this TLV-TWA level).

The OEHHA of the California EPA has proposed to revise its chronic REL and develop an acute REL based on recently available studies. The proposed chronic REL is based on a more recent study (Rogers et al, 1993) in which pregnant mice were exposed to methanol vapours at concentrations ranging from 1000 ppm to 15,000 ppm ($1310 \text{ mg}/\text{m}^3$ to $19650 \text{ mg}/\text{m}^3$) for 7 hours per day on days 6-15 of gestation. Significant increases in the incidence of exencephaly (brain formed outside skull) and cleft palate were observed at $6550 \text{ mg}/\text{m}^3$ and other higher concentrations. A dose-related increase in the number of fetuses per litter with cervical ribs (usually small ossification sites) was observed at $2620 \text{ mg}/\text{m}^3$ and above. A NOAEL of $1310 \text{ mg}/\text{m}^3$ (1000 ppm) was determined for the pregnant mice. After applying a conversion factor for a human equivalent concentration (a default modification factor of 1 for the lack of data for gas:respiratory conversion) and a total uncertainty factor of 30 (3 for interspecies variability and 10 for intraspecies sensitivity), a revised chronic inhalation reference exposure level of $10 \text{ mg}/\text{m}^3$ ($10000 \mu\text{g}/\text{m}^3$) has been proposed. The OEHHA also calculated a maximum likelihood estimate (MLE_{05} ; using a log-logistic model for 5% added risk above background) of $1079 \text{ mg}/\text{m}^3$ (824 ppm) and a benchmark concentration (BMC_{05}) of $400 \text{ mg}/\text{m}^3$ (305 ppm). The observation of a NOAEL and the demonstration of a dose-response relationship are major strengths of the proposed REL. Major weaknesses are the lack of human data for chronic inhalation exposure, the lack of long-term multiple dose studies, and the difficulty in addressing reproductive short-term effects within the chronic REL framework used by the California OEHHA.

The proposed acute inhalation REL of $28 \text{ mg}/\text{m}^3$ of California is based on the human study of Cook *et al.* (1991 as cited in OEHHA, 1998) in which mild adverse effects on 12 young male volunteers were measured after exposure to methanol vapours at $250 \text{ mg}/\text{m}^3$ for a 75 minute period. This pilot study, sponsored by the Health Effects Institute, was designed to simulate potentially worst-case exposure from normal use of methanol-fuelled vehicles. The subjects were administered a battery of 20

commonly used tests of sensory, behavioural and reasoning performance before, during and after exposure. Methanol had no significant effect on the subjects' performance for all but two of the tests. Performance was slightly impaired in one test measuring memory and concentration, and brain wave patterns changed slightly in a test measuring response to light flashes and sounds. Subjects also reported higher levels of fatigue, but the changes did not affect the subjects' ability to maintain vigilance or to respond quickly to stimuli. Strengths of the proposed acute toxicity REL are the human (inhalation) data and the determination of a NOAEL (250 mg/m³ or 192 ppm). An uncertainty factor of 10 was used to account for intraspecies sensitivity. The acute REL is calculated to be 28000 µg/m³ (21 ppm). The only exposure concentration tested was considered a free-standing NOAEL for subtle neurologic effects. Major weaknesses are due to the inherent small sample size of a pilot study and the use of a single dosage level. The California EPA will likely reevaluate their proposed acute toxicity REL when a study of the neurobehavioural effects of methanol using a larger sample size becomes available.

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for methanol. The State recognises that the US EPA's RfC for methanol is currently under review (ARB, 1996). Methanol is not listed under Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996).

Methanol is identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment," which is the State's next step in establishing a potential air quality guideline value (ARB, 1997).

9. Key Risk Management Considerations:

Not applicable.

10. Multimedia Considerations of Guidelines:

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Methanol is not one of these substances.

11. Other Relevant Factors:

Methanol is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program. Annual average concentrations of methanol must also be measured, calculated and/or reported by the State, as well as any facility posting emissions, in order to be used in the analysis of cancer risk and/or chronic non-cancer effects.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Methanol (CAS# 67-56-1)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) is $7.13 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The Allowable Ambient Limit (AAL) is $7.13 \mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1987. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US

EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of methanol, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH occupation exposure limit for methanol, has adopted the level of 200 ppm (equivalent to 262 mg/m³, assuming 25°C, 1 atmosphere, and molecular weight of 32.04 g/mol). For use in the MDEP air guidelines, this level was considered the Most Appropriate Occupational Limit (MAOL) and adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This converts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week to 24 hours per day, seven days per week.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 10 to account for a lack of data or inadequacies in the toxicity database used to review the potential toxicity of methanol.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, $4.2 \times 1.75 \times 10 \times 10 = 735$. The adjusted MAOL is numerically equivalent to $262 \text{ mg/m}^3 / 735 = 0.356 \text{ mg/m}^3 = 356 \text{ }\mu\text{g/m}^3$. At this point, another set of uncertainty factors were applied to the adjusted MAOL:

- I. divided by 10. This is an uncertainty factor which accounts for documented developmental or reproductive effects that methanol exhibits as teratogenic toxicant (MDEP, 1990) but which, as yet, have been unaccounted for in the health assessment.

-
- II. divided by 5 to account for exposure through other media sources. This is based on an assumption that ambient air represents only 20% of the total exposure

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 36,750. The TEL was, therefore, calculated as $7.13 \mu\text{g}/\text{m}^3$.

Non-Threshold Effects

The MDEP reported that there was insufficient evidence to classify methanol's carcinogenic or mutagenic potential (MDEP, 1990). The non-threshold effect exposure limit (NTEL) was developed from the adjusted MAOL ($356 \mu\text{g}/\text{m}^3$) using a non-threshold effects uncertainty factor (NTEUF) of 1. No adjustment was made for multimedia considerations. The resulting NTEL was calculated as $356 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the TEL for methanol of $7.13 \mu\text{g}/\text{m}^3$ was adopted as the AAL.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end-point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

The adjusted MAOL used as the basis of the guideline was divided by 5 to allow for contributions from sources of exposure other than air.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Methanol (CAS # 67-56-1)
2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)
3. *Guideline Value(s):*
The 1-hour Initial Threshold Screening Level (ITSL) is 3,250 $\mu\text{g}/\text{m}^3$.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the Air Toxic Rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices. Sixth Edition. American Conference of Governmental Industrial Hygienists Inc. Cincinnati, Ohio.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL. Specifically, information from the American Conference of Governmental Industrial Hygienist's (ACGIH) process for development of Threshold Limit Values (TLVs), upon which the ITSL for methanol is based, were employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for methanol was determined from the TLV established by the ACGIH and has an averaging time of 1 hour. The ITSL was determined by dividing the occupational exposure level (OEL) (in this case, the ACGIH TLV) by 100. The 100 fold safety factor is derived as follows:

$$\text{ITSL} = \text{OEL} \times \frac{40 \text{ hours}}{168 \text{ hours}} (\text{A}) \times \frac{30 \text{ years}}{70 \text{ years}} (\text{B}) \times \frac{1}{10} (\text{C}) = \frac{\text{OEL}}{100}$$

where:

A adjusts for the difference between a 40 hour work week and the total hours in a week;

B adjusts for the difference between the number of years a person is assumed to work and the assumed lifetime;

C adjusts for the possible higher susceptibility of certain individuals in the general population when compared to healthy adult workers.

The ACGIH established a TLV-STEL (Threshold Limit Value-Short-Term-Exposure-Limit) of 250 ppm for methanol (ACGIH, 1991). TLV-STELs refer to airborne concentrations of substances to

which workers can be exposed continuously for a short period of time without suffering from irritation, chronic or irreversible tissue damage or narcosis of a significant degree. TLV-STELs are recommended only when toxic effects have been reported from high short-term exposures in either humans or animals.

With a conversion factor of $1 \text{ ppm} = 1.3 \text{ mg/m}^3$, 250 ppm is equivalent to 325 mg/m^3 or 325,000 mg/m^3 . This was divided by 100 to arrive at the ITSL of $3,250 \text{ mg/m}^3$.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Methanol (CAS # 67-56-1)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey has not identified a specific air concentration guideline value for methanol. The New Jersey Bureau of Air Quality Evaluation (BAQEv) bases its guideline values on the information made available from the US EPA and other sources. A reference concentration (RfC) of 620 $\mu\text{g}/\text{m}^3$, based on the reference exposure level outlined under the State of California's Committee of the California Air Pollution Control Officers Association (CAPCOA) 1993 Risk Assessment Guidelines has been adopted by the NJDEP (NJDEP, 1997).

4. *Application:*

The BAQEv Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available:*

NJDEP, 1994. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1997. Memorandum regarding the revision of Reference Concentration List. Department of Environmental Protection.

Key Reference(s):

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. Key Risk Assessment Considerations:

The State adopted the State of California's chronic REL of $620 \mu\text{g}/\text{m}^3$. This risk-based reference level is based on the ACGIH TLV-Time-Weighted-Average (TLV-TWA) for methanol. The derivation of this level is detailed in section 11.2 State of California.

9. Key Risk Management Considerations:

Not applicable.

10. Multimedia Considerations of Guidelines:

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. Unit risk factors (URFs) must be used to calculate inhalation risks for carcinogens, while potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, RfCs must be used for inhalation exposure, and reference doses (RfDs) are used for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. Other Relevant Factors:

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Methanol (CAS# 67-56-1)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

No Short-term Guideline Concentration (SGC) has been reported. An interim Annual Guideline Concentration (AGC) 6,200 $\mu\text{g}/\text{m}^3$ has been recommended (NYSDEC, 1992).

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

NYSDEC, 1992. Memorandum to Matt Reis, Bureau of Application Review and Permitting, dated March 25, 1992. Subject: Toxicity Classification of Methanol. Author: Carlos Montes, Bureau of Air Research. New York State Department of Environmental Conservation. Albany, New York.

Key Reference(s):

NIOSH, 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. Status of Guideline(s):

Current.

8. Key Risk Assessment Considerations:

Methanol is classified as a low toxicity air contaminant (NYSDEC, 1992).

The factor used to adjust the occupational limit is based on extrapolating an 8 hour/day, 5 days/week occupational exposure to a 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2). To compensate for applying occupational guidelines to the general population in establishing an AGC, an additional factor of 10 is used for contaminants defined as low toxicity chemicals and a factor of 100 is used for contaminants defined as moderate toxicity chemicals.

For methanol, the interim AGC was developed from the NIOSH REL and an adjustment factor for low toxicity air contaminants of 42 (i.e. 4.2×10).

$$260 \text{ mg/m}^3 / 42 = 6.2 \text{ mg/m}^3 = 6,200 \text{ } \mu\text{g/m}^3$$

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. Multimedia Considerations of Guidelines:

The NYSDEC guideline considers only human exposure to contaminants in air.

11. Other Relevant Factors:

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Methanol (CAS # 67-56-1)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

None.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No.

23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*

Not applicable.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Methanol (CAS # 67-56-1)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Methanol is classified as a class 3 gaseous organic substance (gO.3). This classification imposes an emission standard of 150,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 3.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility-specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. *Peer-Review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 150,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 3.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

9. *Key Risk Management Considerations:*

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Methanol (CAS# 67-56-1)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline available.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. Chemosphere 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No information available.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1,000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} .

No assessment has been carried out for methanol.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

None.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Methanol (CAS # 67-56-1)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. Methanol has not been assessed or evaluated under the first Priority Substance List (PSL1). It was nominated as a substance for consideration, but was not recommended for evaluation by the Ministers' Expert Advisory Panel under the Second Priority Substance List (PSL2).

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
METHYLETHYL KETONE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years (MOEE, 1996). Methyl ethyl ketone (MEK) was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing standard in 1974. A review of scientific and technical information relevant to setting air quality standard for MEK has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for MEK.

Methyl ethyl ketone (MEK; CAS # 78-93-3) is a clear, colourless substance with a sweet, acetone-like odour. Its odour threshold ranges between 5.9 and 251 mg/m³. Methyl ethyl ketone is primarily used by the vinyl, acrylic and textile industries as a protective coating agent. It is also used in the manufacturing of adhesives and magnetic tapes, printing inks, paint, extraction solvents, and in oil dewaxing. Data from the Canadian National Pollutant Release Inventory (NPRI) for the reporting years 1993 to 1997 indicate that MEK was almost exclusively released to air. MEK has been among the top air pollutants in terms of atmospheric release volumes. No consistent pattern in the amount of releases was observed between the years 1993 to 1997.

Data collected in 1993 to 1995 from nine ambient air monitoring stations located across Canada indicated a mean concentration of 1.25 µg/m³ (24-hour average). Five sites in Ontario were part of this nation wide monitoring program. The mean concentrations of these sites were found to range from 1.42 µg/m³ in Ottawa, to 3.20 µg/m³ in Windsor.

Methyl ethyl ketone can be absorbed through the lungs, skin, and gastrointestinal tract. MEK vapours can cause effects including irritation of the eyes, nose and throat, nausea, headaches, vomiting, dermatitis, and it can effect the central nervous system. Acute exposures, up to 588 mg/m³ for three to five minutes, can result in irritation of the eyes and nose. A 4-hour inhalation exposure of 590 mg/m³ of MEK did not show significant effects in a variety of behavioural tests. Chronic adverse effects include headache, dermatitis, gastrointestinal upset, loss of appetite and weight, muscular hypotrophy, as well as numbness of the fingers and arms.

There is a large variation in the susceptibility of experimental animals to MEK. In rats, the lowest lethal concentration of MEK was found to be 2,000 ppm (5,900 mg/m³), whereas guinea pigs exposed to 3,300 ppm (9,735 mg/m³) showed no signs of adverse effects and survived at exposures up to 10,000 ppm (29,500 mg/m³). Chronic exposures induce adverse systemic effects such as enlargement of the

liver (> 760 ppm or $2,242 \text{ mg/m}^3$), developmental effects such as decrease of mean fetal body weight or some degree of malformation ($> 3,000$ ppm or $8,850 \text{ mg/m}^3$), and/or behavioural effects such as slight decrease in visual response rate ($1,000$ ppm or 2950 mg/m^3).

There is inadequate information to evaluate the carcinogenicity of methylethyl ketone in humans. MEK has been shown to potentiate the polyneuropathy effects (degeneration of nerves) of hexacarbon solvents (e.g. *n*-hexane) and haloalkane solvents in humans and animals.

The current Ontario air quality standards ($31,000 \text{ }\mu\text{g/m}^3$) for MEK are set on the basis of odour for both the half-hour Point-of-Impingement (POI) standard and the one-hour Ambient Air Quality Criterion (AAQC). In the process of revising the air quality standards for Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the United States Environmental Protection Agency (US EPA), the States of California, New York, New Jersey, Michigan, and the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

The Commonwealth of Massachusetts, along with the States of New Jersey, Michigan, New York, and California, have either promulgated or proposed air quality guidelines for MEK based on the US EPA Inhalation Reference Concentration (RfC) of 1 mg/m^3 ($1,000 \text{ }\mu\text{g/m}^3$). This RfC is based on the developmental effects in mice. California has derived a short-term (acute) REL value of $26,000 \text{ }\mu\text{g/m}^3$ based on human volunteer studies.

Of the criteria reviewed from these agencies, the Ministry evaluated and accepted the scientific studies which support the development of the Reference Concentration (RfC) of $1,000 \text{ }\mu\text{g/m}^3$ established by the US EPA and the RfC-derived chronic REL from the California EPA. The RfC/REL was developed based on developmental effects and therefore can be considered for a 24-hour averaging AAQC. Given the range of reported odour thresholds (between $5,900$ and $251,000 \text{ }\mu\text{g/m}^3$), the odour effect of MEK is not considered an appropriate rationale for the development of an half-hour point of impingement standard for Ontario.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for MEK:

- **a 24-hour average AAQC of $1,000 \text{ }\mu\text{g/m}^3$ (micrograms per cubic metre of air) for methylethyl ketone based on the adverse health effects of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $3,000 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $31,000 \mu\text{g}/\text{m}^3$ to the proposed level of $3,000 \mu\text{g}/\text{m}^3$, meeting this proposed standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$3,000 \mu\text{g}/\text{m}^3$ to $30,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methylethyl ketone based on the adverse health effects of this compound.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Methylethyl ketone (MEK) was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing standard. A review of scientific and technical information relevant to setting an ambient air quality standard for MEK had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending an AAQC and a POI standard for MEK.

2.0 General Information

2.1 Physical and Chemical Properties

The following list provides some general information on MEK and its properties:

CAS #	78-93-3
RTECS #	EL6475000
UN #	1193
Conversion Factors	1 ppm = 2.95 mg/m ³ @ 25 °C and 1 atm. 1 mg/m ³ = 0.34 ppm @ 25 °C and 1 atm.
Boiling Point	79.6°C
Flash Point	-6°C
Henry's Law Constant	4.16 to 6.11 x 10 ⁻⁵ atm m ³ /mol @ 25 °C
Log K _{OW}	0.29
Formula	C ₄ H ₈ O
Molecular Weight	72.10 g/mol
Vapour Density (air = 1)	2.41
Vapour Pressure	98.0 mm Hg @ 25°C
Common Synonyms	2-Butanone, methyl acetone, MEK

Methylethyl ketone is a clear, colourless substance with a sweet, acetone-like smell. The odour threshold, for this compound ranges from 5.9 to 251 mg/m³, with a geometric mean value of 47 mg/m³ (AIHA, 1989).

2.2 Uses

Today, MEK is primarily used by vinyl, acrylic and textile industries as a solvent in protective coating agents (US EPA, 1994). It is also used in the manufacturing of adhesives and magnetic tapes, printing inks, paint and extraction solvents, and also in oil dewaxing (HSDB, 1997). Traditionally, MEK has been used as an extraction solvent in the food industry, a sterilization solvent in the medical industry, and a synthetic agent in the pharmaceutical and cosmetic industries (US EPA, 1994).

2.3 Sources and Levels

Sources

MEK occurs naturally in a number of food and beverage products. It is released into the environment from industrial and domestic uses. The largest sources that release MEK to the environment are the coatings, resins and adhesives industries (US EPA, 1994). Away from industrial areas, major sources of MEK are vehicle exhausts and photochemical reactions. Cigarette smoke and other tobacco products also contribute to individual exposures (WHO, 1993). Indoor air levels, of MEK can be much higher than ambient air levels (WHO, 1993). Although MEK can be found in foods and drinking water, air is the major route of exposure (WHO, 1993).

Environment Canada's National Pollutant Release Inventory (NPRI) summarises the emissions of chemicals in Canada based on information provided by reporting facilities (NPRI, 1993, 1994, 1995, 1996 & 1997). Data obtained from the NPRI reports of 1993 to 1997 indicates that MEK has been among the top 8 pollutants, as a result of atmospheric release volumes in these three years. There were about 120 to 140 sources of MEK emission in Canada, of these, more than 62% were in Ontario. The annual atmospheric releases of this compound were 3356, 4234 and 4080, 4450 tonnes in 1993, 1994, 1995 and 1996, respectively. In 1997, 4429 tonnes of MEK were released from 135 sources across Canada. However, no consistent pattern of releases was observed in Canada. Similarly, atmospheric emissions of MEK in Ontario showed no discernable pattern. There were 2842, 3568, 3330, 3678 and 3607 tonnes of MEK released, to the air in Ontario for the years of 1993, 1994, 1995, 1996 and 1997, respectively. Ontario emissions constituted approximately over 80% of the national atmospheric releases. Most of the releases in these years were attributed to industries of petroleum, rubber, plastic, paper and allied products, wall covering, textile products, wood and chemical products, furniture and fixture, automotive and parts industries.

Ambient Air Concentrations

Environment Canada collected ambient air data for MEK from January 1993 to December 1995 for nine monitoring stations across Canada. The 24-hour average concentration of $1.25 \mu\text{g}/\text{m}^3$ was observed for these nine stations. The concentrations reported ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $14.72 \mu\text{g}/\text{m}^3$. Five sites in Ontario were monitored during this period, reporting mean concentrations of MEK ranging from $1.42 \mu\text{g}/\text{m}^3$ in Ottawa to $3.20 \mu\text{g}/\text{m}^3$ in Windsor (Environment Canada, 1997). Monitoring by the Ministry found that half-hour average concentrations of MEK in Ontario ranged from 1 to $800 \mu\text{g}/\text{m}^3$ (MOEE, 1997a). Maximum levels were detected at an industrial plant in Port Hope in 1993 ($800 \mu\text{g}/\text{m}^3$) and an industrial plant in Cornwall in 1992 ($620 \mu\text{g}/\text{m}^3$) (MOEE, 1997a).

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 129 facilities that emitted MEK were examined. These approvals were for emissions from industries in automotive spray paint and parts, adhesives, plastic and metal products. The median Ground Level Concentration estimated by Regulation 346 dispersion modelling for all 129 sources was approximately $61.54 \mu\text{g}/\text{m}^3$. The maximum and minimum were 8859 and $0.013 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

Methylethyl ketone occurs naturally at low concentrations in air, water and soil. It is highly mobile in the natural environment and is not accumulated in any individual compartment (WHO, 1993). Once released into the atmosphere, MEK breaks down by photochemical degradation (HSDB, 1997). The half-life of MEK from the reaction with photochemically formed hydroxyl radicals has been estimated to be 2.3 days (US EPA, 1994). Direct photolytic degradation will also occur with a calculated half-life of approximately 15.4 hours (US EPA, 1994). Deposition by rain or fog might also play a minor role in the removal of MEK released into the atmosphere (HSDB, 1997). MEK released to water is expected to rapidly volatilise to the atmosphere (HSDB, 1997). MEK is rapidly metabolized by bacteria, mammals and other organisms. Bioconcentration of MEK in fish or aquatic organisms is not expected, as the estimated fish bioconcentration factor for MEK is less than one (US EPA, 1985).

3.0 Toxicology of Methylethyl Ketone

The following toxicological review of MEK is primarily focussed on the inhalation route of exposure, as this pathway appears to be the major route of intake in humans and since this rationale document is concerned with the development of air standards. Data on other exposure media are included where relevant or where inhalation data are lacking.

Methylethyl ketone can be absorbed through the lungs, skin and gastrointestinal tract. About 41 to 56% of MEK is taken up by pulmonary absorption (US EPA, 1994). There appears to be an even and widespread distribution of MEK in human tissues, with similar concentrations found in the kidney, liver, brain, heart, lung, and in fat and muscle tissue (US EPA, 1994). MEK is metabolized by oxidative hydroxylation in guinea pigs and rats, forming 3-hydroxy-2-butanone, which is further reduced to 2,3-butanediol. MEK has also been shown to be reversibly reduced to 2-butanol (US EPA, 1994). In humans, about 30 to 40% of the inhaled MEK is expired to air. Both unmetabolized MEK and its metabolite, 3-hydroxy-2-butanone have been measured in the urine of exposed workers, although the metabolite was only identified in workers exposed to higher levels ($\sim 272 \text{ mg}/\text{m}^3$). An estimate of the plasma half-time in humans is 49-96 minutes, with a clearance rate of $0.6 \text{ L}/\text{minute}$ (US EPA, 1994).

3.1 Acute Toxicity

Adverse effects of MEK vapours include irritation of the eyes, nose and throat, nausea, headaches, vomiting, dermatitis, and it affects the central nervous system. Exposure to 588 mg/m³ MEK, for 3 to 5 minutes resulted in irritation of the eyes and nose (as reviewed in Calabrese and Kenyon, 1991). A 4-hour inhalation exposure to 590 mg/m³ MEK did not have significant effect in a variety of behavioural tests including psychomotor, visual vigilance, dual task, sensorimotor and psychological tests ((Dick, *et al.* 1992, as cited in OEHHA, 1998 and reviewed in WHO, 1993). Extreme nausea and vomiting are accompanied by peripheral neuropathy following doses of about 1,470 mg/m³ or more, after 0.5-1 hour exposures (as reviewed in HSDB, 1997). Human volunteers exposed to 270 ppm (780,000 µg/m³) of MEK for two hours experienced eye, nose, and throat irritation, as well as lacrimation and sneezing (Nakaaki, 1974 as cited in OEHHA, 1998).

Data from inhalation exposure studies in animals indicated that the acute toxicity of MEK is low (see WHO, 1993). The LC₅₀ (concentration lethal to half of the experimental animals) (45-min.) in male CF1 mice was found to be 205,000 mg/m³ ± 32,500 mg/m³ (69,500 ± 11,000 ppm) and in male albino rats the LC₅₀ (4-hour) was 34,500 mg/m³ (11,700 ppm). The lowest lethal concentration of MEK, for rats as result of inhalation exposure (4-hour) was found to be 2,000 ppm (5,900 mg/m³) whereas guinea pigs exposed to 3,300 ppm (9,735 mg/m³) showed no signs of adverse effects, and survived up to a MEK concentration of 10,000 ppm (29,500 mg/m³). Concentration-related decreases in response to visual stimulus in male Charles River CD1 mice were observed at 2,950 - 29,500 mg/m³ (1,000 - 10,000 ppm) MEK in a two and a half-hour exposure period. Respiratory irritation occurred within 2 min. in guinea pigs exposed to MEK at 29,500 mg/m³ (as reviewed in WHO, 1993).

3.2 Subchronic and Chronic Toxicity

Repeated or prolonged exposure to relatively high concentrations of MEK vapours has resulted in adverse central nervous system effects in humans. Limited chronic occupational exposure data indicated that workers exposed to 882 to 1,764 mg/m³ MEK experienced numbness in the fingers and toes. In another study workers chronically exposed to the chemical showed signs of neurotoxicity, with decreased nerve conduction velocities, headaches, dizziness, dermatitis, gastrointestinal upset, loss of appetite, and loss of weight, and muscle hypotrophy, with the absence of clinically recognizable neuropathy (as reviewed in WHO, 1993; US EPA, 1994). Severe pulmonary irritation may accompany central nervous system depression when exposed to high concentrations of MEK.

Chronic inhalation exposure of animals to MEK indicated low compound-related toxicity (see WHO, 1993). Rats of both sexes exposed to MEK at 14,750 mg/m³ (5000 ppm) for 6 hours/day, 5 days/week for 90 days showed small increases in liver weight; slight decreases in brain and spleen

weights and slightly altered blood chemistry in female rats. Exposure of rats to MEK at 3,700 to 14,870 mg/m³ (1254 to 5041 ppm) for 6 hours/day, 5 days/week for 90 days had no effects on food consumption or the nervous system. Rats exposed to 2,242 and 2,360 mg/m³ (760 and 860 ppm) of MEK for 6 hours/day, 5 days/week for 4 weeks showed some signs of liver enlargement (as reviewed in WHO, 1993).

3.3 Developmental and Reproductive Toxicity

MEK has been implicated as causing fetal toxicity and possibly adverse developmental effects in animals. Sprague-Dawley rats were exposed to 0, 3,310, or 11,007 mg/m³ MEK vapour for 7 hours/day on days 6 to 15 of gestation. Fetal body weight and crown-rump length were significantly decreased at the low (but not the high) exposure level, and dose-related increases in skeletal anomalies were observed (as reviewed in Calabrese and Kenyon, 1991). Inhaled MEK induced adverse developmental effects in mice. Pregnant mice were exposed to 0, 1,170, 2,969, or 8,879 mg/m³ MEK vapour for 7 hours/day during days 6-15 of gestation. Decreased fetal body weight was observed at the highest dose level. An increased incidence of malformations in the fetuses and litters of the treated groups was seen, but they were not found to be statistically significant results (as reviewed in US EPA, 1994; US EPA, 1997; WHO, 1993).

3.4 Genotoxicity

Methylethyl ketone does not appear to be mutagenic. The chemical was found to be non-mutagenic to several strains of *S. typhimurium* and *E. coli* strain WP2 (as reviewed in Calabrese and Kenyon, 1991). MEK was also negative in the mouse lymphoma test, the cell transformation assay, and the mouse and Chinese hamster micronucleus tests *in vivo* (as reviewed in US EPA, 1994). MEK was negative in a mitotic gene conversion assay with *S. cerevisiae*; however, MEK was reported to cause chromosomal nondisjunction in *S. cerevisiae* (as reviewed in Calabrese and Kenyon, 1991; WHO, 1993).

3.5 Carcinogenicity

In its health assessment of MEK, the US EPA concluded that there is inadequate information to evaluate the carcinogenicity of MEK (US EPA, 1997). An epidemiological study of 446 male workers in two MEK dewaxing plants revealed no excess cancer incidence. Overall, deaths from cancer were below the expected rate. A small increase in tumours in the mouth and throat was seen (2 observed, 0.13 expected) and lung cancers were significantly decreased (1 observed, 6.02 expected) (as reviewed in WHO, 1993; US EPA, 1994). No increases in mouth and throat cancers were seen in a study of 1,008 male oil refinery workers, exposed to 2.94 to 11.8 mg/m³ MEK. The overall deaths from cancer were also less than expected (as reviewed in US EPA, 1994). MEK applied to the skin of

mice twice weekly, for one year at the rate of 50 mg/dose did not produce any tumours (as reviewed in US EPA, 1994).

3.6 Methylethyl Ketone in Solvent Mixtures

Effects of inhalation exposure of humans to MEK and other simultaneously present organic solvents were examined since MEK was a common component of solvent mixtures. However, studies on the interaction of MEK with hexacarbon solvents through occupational exposures were limited. In one study, 95 workers, 24 males and 71 females, ranging in age from 16 to 62 (mean age, 30.9 ± 11.7 years) and ranging in exposure durations from 1 to 25 years (mean, 9.1 ± 8 years) from an Italian shoe factory were studied. Over a 2-year period, the concentrations of the various solvents in the breathing area were: MEK, 115 mg/m^3 (39 ppm); *n*-hexane, 317 mg/m^3 (90 ppm); cyclohexane, 315 mg/m^3 (92 ppm); ethyl acetate, 205 mg/m^3 (57 ppm). The exposed workers complained of sleepiness, dizziness, weakness, paresthesia (abnormal sensation), and hypo-esthesia (as reviewed in WHO, 1993; US EPA, 1994). In addition, the mean motor nerve conduction velocity in these workers was significantly reduced in the median and peroneal nerves but not in the ulnar nerve. The amplitude of the motor action potential was significantly reduced in all nerves and its duration was increased in the ulnar nerve. There were no significant changes in the distal latency. The number of abnormal action potentials in the median and peroneal nerves was significantly increased. A correlation between the reduction in motor conduction velocity and exposure was observed.

In a follow-up study, 15 female shoe factory workers, aged 19-53 years (mean age, 26.6 ± 11.4 years) and an exposure duration of 2 - 8 years (mean, 4.5 ± 2.3 years) were examined for electrophysiological changes. The concentrations of the various solvents in the breathing area were: MEK, 177 mg/m^3 (60 ppm); *n*-hexane, 690 mg/m^3 (196 ppm); cyclohexane, 585 mg/m^3 (170 ppm); ethyl acetate, 360 mg/m^3 (100 ppm). It was observed that in the peripheral nerves significant reductions in maximal motor and distal sensory nerve conduction velocities in the median and ulnar nerves and reduced maximal motor nerve conduction velocity in the peroneal nerve. The latency of the sensory peak action potential in the median and ulnar nerves were significantly increased. The amplitude of the action potentials of all peripheral nerves were slightly reduced. Changes in the evoked potentials of the somatosensory nerve were also noted. The latency of some early component peaks was significantly increased and the amplitude of some of the early peaks was significantly reduced. It was suggested that the neurotoxicity of the solvent mixture was primarily attributable to *n*-hexane (as reviewed in WHO, 1993).

In Germany during 1974, two thousand cases of solvent abuse, which resulted in severe polyneuropathy, led to research on the potential of MEK to enhance the adverse health effects of *n*-hexane, and on the interactions of MEK with other hexacarbon solvents (as reviewed WHO, 1993). Victims of solvent abuse often found development of paresthesia and weakness in leg and arm muscles.

Neurophysiological and histological findings indicated reduction in motor and sensory nerve conduction velocities, and were in proportion to the degree of paresis. Damage to the nerves was also reported. The outbreak of neuropathy in solvent abuse victims coincided with the change of solvent formulation from one with *n*-hexane, benzene fraction, ethyl acetate and toluene to a similar solvent mixture with less (16%) *n*-hexane and the addition of 11% MEK. It was suggested that MEK enhanced the neuropathy of *n*-hexane.

The report of a case of severe sensorimotor neuropathy in a fabric factory in the U.S.A. led to a thorough investigation of effects of MEK in solvent mixtures. Eighty six of the 1,157 workers examined reported signs and symptoms of peripheral neuropathy, including paresthesia in arms and legs and weakness in the hands and legs. It was noted that prior to the confirmation of the first case, methylbutyl ketone had been substituted for methylisobutyl ketone as a co-solvent with MEK. The concentrations in the greatest exposure areas for MEK were 251 - 2,251 mg/m³ (85 - 763 ppm) and for methylbutyl ketone were 9 - 640 mg/m³ (2.3 - 156 ppm). It was suggested that methylbutyl ketone may be responsible for the observed neuropathy. Results from an animal study suggested that concurrent exposure to MEK accelerated methylbutyl ketone-induced neuropathy (WHO, 1993).

It has been demonstrated that MEK enhanced the neurotoxicity of *n*-hexane in animals under continuous exposure conditions (as reviewed in US EPA, 1997 & ATSDR, 1997 and WHO, 1991). *n*-Hexane-induced hindlimb paralysis and related neuropathology were manifest after 9 weeks in all 5 Wistar rats exposed continuously to *n*-hexane at 1,760 mg/m³ (500 ppm), 22 hours/day, 7 days/week. These clinical signs were present 1 week earlier in animals exposed to mixtures of 1,056 mg/m³ (300 ppm) *n*-hexane with 590 mg/m³ (200 ppm) MEK and 1,408 mg/m³ (400 ppm) *n*-hexane with 295 mg/m³ (100 ppm) MEK. Exposure to 1,760 mg/m³ *n*-hexane and 590 mg/m³ MEK resulted in complete hindlimb paralysis after 4 weeks. Rats exposed to *n*-hexane at 2464 mg/m³ (700 ppm) or 1760 mg/m³ *n*-hexane + 590 mg/m³ MEK for 8 hours/day, 7 days/week for 40 weeks did not show clinical signs of neuropathy. It appears that MEK enhanced the neurotoxic effect of *n*-hexane (shortened onset of neuropathological effect of *n*-hexane) under continuous exposure conditions, but not under intermittent exposures.

It is necessary to understand the possible mode of action of hexacarbon solvents in inducing neuropathy before studying the likely mechanism of MEK in the potentiation of the neurotoxic effects of these solvents. It has been postulated that methylbutyl ketone and *n*-hexane both can be oxidized by hepatic microsomal enzymes to 2,5-hexanedione, the proximate neurotoxicant. The 2,5-hexanedione formed may induce cross-linking of neurofilaments, blocking the transport at the node of Ranvier and swelling from accumulated neurofilaments proximal to the nodes and axonal degeneration distal to the nodes. In animal studies it was found that if the concentrations or doses of *n*-hexane, methylbutyl ketone or 2,5-hexanedione were high enough and sustained for long enough periods of time, clinical signs of neural

degeneration were evident and neural degeneration was made more severe (or the onset of neuropathy was often shortened) by co-exposure to MEK (as reviewed in WHO, 1993).

Although MEK enhanced the neurotoxic effects of *n*-hexane and methylbutyl ketone, and was frequently observed in rats *in vivo*¹, information on the mechanism of action for MEK has not been well described. There were some suggestions that MEK may have metabolic interaction with *n*-hexane and methylbutyl ketone (as reviewed in WHO, 1993). Simultaneous inhalation exposure of *n*-hexane and MEK resulted in lower levels of 2,5-hexanedione (a common metabolite of *n*-hexane and methylbutyl ketone) in urine of rats *in vivo*, and initially lower followed by somewhat elevated levels of methylbutyl ketone and 2,5-hexanedione in serum *in vivo*. However, the increased 2,5-hexanedione level alone cannot explain the potentiation of *n*-hexane neurotoxicity. It appears that MEK may be involved in the activation of some components in the metabolism of *n*-hexane. Pretreatment of rats with MEK prior to inhalation exposure to *n*-hexane resulted in higher levels of 2,5-hexanedione in several tissues, including blood. It has been reported that in rats an 8-hour simultaneous exposure to MEK and methylbutyl ketone did not result in noticeable levels of methylbutyl ketone or 2,5-hexanedione in blood, whereas a 6-day continuous co-exposure resulted in substantially higher levels of methylbutyl ketone and 2,5-hexanedione. However, continuous co-exposure for 23 days resulted in further elevation of methylbutyl ketone in blood, but no measurable level of 2,5-hexanedione. In guinea pigs, intraperitoneal administration of a mixture of MEK/methylbutyl ketone raised the levels of 2-hexanol, a common intermediate metabolite of methylbutyl ketone and *n*-hexane, but had no effect on the levels of this metabolite when methylbutyl ketone was administered alone (as reviewed in WHO, 1993).

At this point there is insufficient information to delineate the mechanism of MEK in enhanced hexacarbon solvent neurotoxicity. It may be of relevance to note that MEK has been demonstrated to potentiate the hepatotoxic effects of haloalkane solvents, such as carbon tetrachloride and chloroform, through a possible mechanism of increased bioactivation of haloalkanes.

3.7 Environmental Effects

The direct application of MEK (0.31 to 0.37 mg) to tsetse flies (*Glossina morsitans morsitans*), caused a marginally increased mortality rate in the treated flies as well as significantly decreasing the activity of treated male flies (but not the female flies) (Kwan et al, 1978). MEK has been found to be quite effective as a fumigant against the Caribbean fruit fly, *Anastrepha suspensa*, as the complete destruction of fruit fly larva was observed following treatment with MEK at 790 mg/m³ for 2 hours or 316 mg/m³ for 7 hours (Davis et al, 1977).

¹ For more information on the MEK potentiated neurotoxic effects of hexacarbon solvents and haloalkanes in animals, see WHO, 1993.

Methylethyl ketone has been shown to affect the germination of several types of seeds. Experimental data indicate that 900 mg/L (in water) of MEK cause a 50% reduction in the germination of lettuce (*Lactuca sativa*) seeds (Reynolds, 1977). Germination of wheat seeds was inhibited when the seeds were treated with 6.4 MEK mg/g seed; only 10% of the treated seeds germinated in comparison with 60% of the control seeds (Nandi et al, 1976).

The toxicity of MEK to aquatic organisms is considered to be low, as 96-hour LC_{50} values range from 3,200 mg/L for fathead minnow (*Pimphales promelas*) (Veith et al, 1983) to 5,600 mg/L for mosquito fish (*Gambusia affinis*) (Wallen et al, 1957). A 48-hour LC_{50} value of 1,382 mg/L has been determined for the water flea, *Daphnia magna* (Union Carbide Corporation, 1980).

Fungi producing MEK can inhibit germination of plants. Growth inhibition of algae caused by MEK ranges from 120 mg/L for blue-green algae (*Cyanobacterium*) to 4,300 mg/L for green algae (*Scenedesmus quadricauda*) (WHO, 1993).

4.0 Existing Air Quality Criteria

4.1 Overview

The current Ontario half-hour POI standard and the 1-hour AAQC for MEK are both set at 31,000 $\mu\text{g}/\text{m}^3$. These criteria were developed based on the odour effect of MEK (MOEE, 1994a).

The documentation from ten agencies (the United States federal government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal government) was reviewed for the existence and basis for their air quality criteria for MEK. A brief summary of this review is presented in Table 1, and agency-specific summaries of information concerning air quality guidelines for MEK are presented in Section 11.0.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE normally uses a factor of 15 to convert from criteria based on annual average concentrations to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Table 1. Summary of Existing Air Quality Guidelines^[1] for MEK

Agency	Guideline Value	Basis of Guideline	Date ^[2]	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration): 1 mg/m ³ (1000 µg/m ³) (lifetime exposure).	Study of developmental effects in mice.	1998	No air guideline promulgated.
California	No current guideline.			MEK appears on the Toxic Air Contaminants Identification List.
	Proposed: acute REL of 26,000 µg/m ³ chronic REL of 1,000 µg/m ³	RfC from US EPA	1998 1997	
Massachusetts	TEL (Threshold Effects Exposure Limits): 200 µg/m ³ (24-hour average).	RfC from US EPA.	1995	Adjusted to allow for exposures via other media.
	AAL ^[3] (Allowable Ambient Limit): 200 µg/m ³ (annual average).	RfC from US EPA.	1997	
Michigan	ITSL (Initial Threshold Screening Level): 1,000 µg/m ³ (24-hour average).	RfC from US EPA.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC: 1,000 µg/m ³ (24-hour average).	RfC from US EPA.	1994	Permitting application. The RfC must be used to assess risks in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): 140,000 µg/m ³ (1-hour average).	TLV-TWA from ACGIH.	1997	Used for permitting.
	AGC ^[4] (Annual Guideline Concentration): 1,000 µg/m ³ .	RfC from US EPA.	1997	Used for permitting.
WHO	None.			
Netherlands	150,000 µg/m ³ (half-hour average).	Emission standard.	1992	Used for permitting.
Sweden	None.			
CEPA	None.			
Ontario	half-hour POI standard: 31,000 µg/m ³ . 1-hour AAQC: 31,000 µg/m ³ .	Both the POI and AAQC are based on odour.	1994	

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.
- Discrepancy in agency guideline has been corrected (MDEP, 1997).
- Discrepancy in agency guideline has been corrected (NYSDEC, 1997).

None of the agencies considered MEK to be a potential carcinogen. Seven of the 10 agencies that were reviewed, (the US EPA, California, the Commonwealth of Massachusetts, the States of Michigan, New Jersey and New York, and The Netherlands), have developed reference values or criteria for MEK. The US EPA has developed a reference concentration (RfC) of $1,000 \mu\text{g}/\text{m}^3$ for MEK. This RfC is based on a study of the developmental effects in mice. This value has been used by various states to set their own criteria. Of the guidelines reviewed, the Massachusetts Department of Environmental Protection (MDEP) makes use of an additional consideration for multimedia exposure (MDEP, 1994).

New York's Short-term Guideline Concentration (SGC) is based on the Threshold Limit Value-Time Weighted Average (TLV-TWA) of the American Conference of Governmental Industrial Hygienists (ACGIH). The State of California has proposed an acute (one-hour) REL of $26,000 \mu\text{g}/\text{m}^3$ (OEHHA, 1998). This was derived from LOAEL observed among four volunteers exposed to an increasing concentration of MEK (90-270 ppm or $260,000$ - $780,000 \mu\text{g}/\text{m}^3$). The Netherlands has set an emission standard for MEK, which is used for permitting applications.

4.2 Review of Existing Criteria

The US EPA (1997) has calculated an inhalation reference concentration (RfC) of $1 \text{ mg}/\text{m}^3$ ($1,000 \mu\text{g}/\text{m}^3$) for MEK. Considered in the derivation of the RfC are the developmental effects based on an inhalation study conducted on mice and reported in different formats by Schwetz *et al.* (1991) and Mast *et al.* (1989). Both a no-observed-adverse-effect-level (NOAEL) and a lowest-observed-adverse-effect-level (LOAEL) were identified.

Groups of 23 to 28 pregnant Swiss mice were exposed to MEK vapours at concentrations of 0, 398, 1,010, or 3,020 ppm (0, 1174, 2980, or $8909 \text{ mg}/\text{m}^3$, respectively) for 7 hours/day during days 6 to 15 of gestation (Schwetz *et al.*, 1991). Dams were killed on gestational day 18 and although a concentration-related increase in relative liver and kidney weight was observed, the difference was statistically significant only at the highest dose level (US EPA, 1997). Neither maternal nor developmental toxicity was exhibited at 1,010 ppm ($2,980 \text{ mg}/\text{m}^3$) or less. At the highest dose group (3,020 ppm or $8,909 \text{ mg}/\text{m}^3$), some mild maternal and developmental effects were observed (LOAEL). A mild decrease in mean fetal body weight was observed, however, it was statistically significant only in male fetuses at the highest dose group. There was a dose-related increase in the incidence of misaligned sternbrae in the fetuses but was only statistically significant at the highest exposure concentration. No significant increase in any single malformation was found. However, some malformations such as cleft palate, fused ribs, missing vertebrae and syndactyly, were observed in one litter of the exposed group.

The US EPA considered 1,010 ppm (2,980 mg/m³) as the no-observed-adverse-effect-level (NOAEL). For developmental effects this agency did not consider an exposure duration adjustment necessary. After applying a total uncertainty factor of 3,000 (10 for interspecies extrapolation, 10 for sensitive individuals, 10 for an incomplete database including a lack of chronic and reproductive toxicity studies, and 3 for lack of unequivocal data for respiratory tract effects) the resulting RfC was 1 mg/m³, or 1,000 µg/m³ (see Section 11.1).

The US EPA identifies as outstanding concerns that insufficient data are presented for possible respiratory effects, despite corroborative principal and supporting studies for a developmental toxicity endpoint. Furthermore, no multi-generational studies were performed and only a single subchronic study was identified. None of the studies reviewed addressed the potential for MEK to cause irritant effects to the upper respiratory tract and nasal regions for short-term exposures at concentrations above the LOAEL. Confidence in the principal study is medium, while confidence in the database and RfC are low (US EPA, 1997). The US EPA last reviewed the RfC for MEK in July of 1992.

The States of Michigan, New Jersey, New York (for their AGC) and the Commonwealth of Massachusetts have promulgated air quality guidelines or RfCs for MEK based on the US EPA's RfC. The state agencies of Michigan, New Jersey and New York adopted the RfC value of 1,000 µg/m³ directly as their respective criteria.

After reviewing the basis of the RfC for MEK, Massachusetts adopted the RfC level of 1.0 mg/m³ (1,000 µg/m³) for use in the MDEP air guidelines. The RfC is used as a starting point for the derivation of the TEL and Non-Threshold Effects Limit (NTEL). For the TEL derivation, the RfC was divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure. The TEL was therefore, calculated as 200 µg/m³. The MDEP reported that there was insufficient evidence to consider the carcinogenic or mutagenic potential of MEK for their guideline development (MDEP, 1990). The NTEL was derived from the US EPA's RfC (1,000 µg/m³) by using a Non-Threshold Effects Uncertainty Factor (NTEUF) of 1. No adjustment was made for multimedia considerations. The resulting NTEL for MEK was calculated as 1,000 µg/m³. Since the AAL is lower than both the TEL or NTEL the value of 200 µg/m³ was adopted as the AAL for MEK.

The State of California has recently proposed to adopt the RfC of 1,000 µg/m³ from the US EPA for its chronic inhalation Reference Exposure Level (REL) (OEHHA, 1997).

New York based its SGC on the ACGIH TLV-TWA limit for MEK of 200 ppm (590 mg/m³). The ACGIH reported that slight nose and throat irritation was found in human subjects exposed to 100 ppm (295 mg/m³) and mild eye irritation in some subjects at 200 ppm (590 mg/m³) (ACGIH, 1991). The ACGIH recommended a TLV-TWA of 200 ppm (590 mg/m³) based on the prevention of injurious

systemic effects and to minimize objections to odour and irritation (ACGIH, 1991). The TLV was adjusted by New York before being applied as an air quality guideline. These adjustments account for the differences from the intended application of the occupational exposure limits, i.e., a healthy adult worker exposed 8 hours/day or 40 hours/week over the course of his or her working life, to a member of the general population (perhaps more sensitive to the effects of a toxic substance) exposed continuously over a lifetime.

The State of California has proposed an acute (one-hour) REL of $26,000 \mu\text{g}/\text{m}^3$ (OEHHA, 1998). This was derived from LOAEL observed among four volunteers exposed to an increasing concentration of MEK between 90-270 ppm or $260,000$ - $780,000 \mu\text{g}/\text{m}^3$ over two hours (Nakaaki 1974, as cited in OEHHA, 1998). The reviewers note that it is unclear if, at the lowest concentration, the only effect was odour perception. However, a mild irritation effect was noted at $780,000 \mu\text{g}/\text{m}^3$ which was considered a LOAEL. In another study of volunteers exposed at 200 ppm ($590,000 \mu\text{g}/\text{m}^3$) no neurological effects or irritation were seen (Dick *et al.*, 1992 as cited in OEHHA, 1998). Uncertainty factors were applied to the LOAEL from the Nakaaki (1974) study, the value 3 was applied to take into account the observation of a mild irritation effect and the value 10 was used to account for variations in sensitivity in humans, for a total uncertainty factor of 30.

The Netherlands has set an emission standard for MEK, for the purpose of permitting applications, of $150,000 \mu\text{g}/\text{m}^3$. The scientific basis for the derivation of this guideline was not available. The WHO, Sweden, and the Canadian Federal Government have not set air quality guideline values for MEK.

In its health assessment of MEK the US EPA (1994) concluded there was insufficient information to evaluate the carcinogenicity of MEK in humans or animals. Due to lack of data, none of the agencies reviewed have considered a carcinogenic end-point in developing a criterion for MEK.

The potentiation effect of MEK in hexacarbon solvent- or haloalkane solvent-induced neuropathy may raise the prospect of health concerns. Since MEK is a common component of solvent mixtures in industrial uses, this effect of MEK should be considered in criteria development.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted Information Draft documents for eighteen chemicals, including MEK, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding the completeness of relevant inhalation toxicological information examined by the Ministry and the rationale of the agency guidelines that the Ministry has considered an appropriate basis for the development of air quality standards, specifically, the use of the RfC of the US EPA and the chronic REL of the California EPA. Finally, the Ministry also requested comments on

technical and economic impacts which may be anticipated as a consequence of the potential revision(s) of the air quality standard.

During the consultation period the Ministry received submissions from various stakeholders regarding the draft document for MEK. Comments from the automobile manufacturing stakeholders explained that their facilities were operating at an estimated GLC of approximately greater than 10% of the MOE's current POI standard and any changes in the current POI may have technical and economic impact to this sector. One automobile equipment and parts manufacturer agreed that the RfC of the US EPA was a reasonable basis for air quality standards development; however, impacts of a revised standard on coating applicators and manufacturers should be examined. The petroleum products stakeholders suggested that a full risk management process may be necessary if the standard for MEK was to be decreased. One automotive paint manufacturer indicated that a substantially reduced POI standard for MEK would not be practical or financially attainable.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (Information Drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for MEK. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted, depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for MEK

The current Ontario half-hour POI standard and the 1-hour AAQC for MEK are both set at 31,000 $\mu\text{g}/\text{m}^3$. These criteria were developed based on the odour effect of MEK.

Based on the rationale for guidelines of the various agencies reviewed, most of the U.S. state agencies support the scientific basis of the RfC developed by the US EPA for MEK. Furthermore, 4 of the 5 agencies studied have adopted this RfC value as the basis for their guideline development; the fifth agency is in the process of doing so.

From the limited data concerning the acute adverse effects of MEK on humans, inhalation of this compound does not appear to induce significant behavioural changes in test subjects (up to 200 ppm or 590,000 $\mu\text{g}/\text{m}^3$ for 4 hours) (WHO, 1993). Chronic occupational exposure to MEK alone may have mild effects on the central nervous system (headache, dizziness), gastrointestinal upset and muscle weakness. Chronic exposure of animals to MEK may induce adverse systemic effects such as enlargement of the liver (> 760 ppm or 2,242,000 $\mu\text{g}/\text{m}^3$), developmental effects such as decrease of mean fetal body weight and some degree of malformation ($> 3,000$ ppm or 8,850,000 $\mu\text{g}/\text{m}^3$), or behavioural effects such as slight decrease in visual response rate (1,000 ppm or 2,950,000 $\mu\text{g}/\text{m}^3$).

All guidelines found are based on the US EPA RfC of 1000 $\mu\text{g}/\text{m}^3$. This guideline was derived from a no-observed-adverse-effect-level (NOAEL) of 1,010 ppm (2,980 mg/m^3) from a study on mice (Schwetz *et al.*, as cited in US EPA 1997). A total uncertainty factor of 3,000 was used. California has derived a short-term REL value of 26,000 $\mu\text{g}/\text{m}^3$ based on human volunteer studies.

The potentiation effect of MEK in hexacarbon solvent- or haloalkane solvent-induced neuropathy may raise an additional prospect for health concerns. Since MEK is a common component of solvent mixtures in industrial uses, this effect of MEK should be considered in criteria development.

Considering the developmental effects and the potentiation of the neuropathological effects of other common solvents, a health effect-based 24-hour AAQC can be derived using the RfC and REL of 1000 $\mu\text{g}/\text{m}^3$ of the US EPA and the California EPA as the basis.

Regarding the broad range of reported odour thresholds which lie between 5,900 and 251,000 $\mu\text{g}/\text{m}^3$ with a geometric mean of 47,000 $\mu\text{g}/\text{m}^3$, the aesthetic effect (i.e. odour) of MEK is not an appropriate rationale for the development of a half-hour POI standard.

8.0 Recommendations

The MOE has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the Reference Concentration (RfC) established by the United States Environmental Protection Agency (US EPA) and the RfC-derived chronic REL proposed by the California EPA. After reviewing additional toxicological information, the Ministry considered that the uncertainty factors used to derive the RfC/REL of $1,000 \mu\text{g}/\text{m}^3$ by these US agencies are appropriate. Since the RfC is derived based on developmental effects, the RfC/REL can be considered for a 24-hour averaging time. Thus, the RfC/REL of $1,000 \mu\text{g}/\text{m}^3$ becomes the health-based 24-hour AAQC. The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour criteria. This factor is derived from empirical measurements and is employed to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). Accordingly, a POI standard of $3,000 \mu\text{g}/\text{m}^3$ would be obtained by multiplying the 24-hour AAQC by a factor of 3.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion for MEK:

- **a 24-hour average AAQC of $1,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methylethyl ketone based on the adverse health effects of this compound.**

Based on supporting science and dispersion modelling, a half-hour POI standard of $3,000 \mu\text{g}/\text{m}^3$ can be derived. However, considering the magnitude of the reduction from the current standard of $31,000 \mu\text{g}/\text{m}^3$ to the proposed level of $3,000 \mu\text{g}/\text{m}^3$, meeting this proposed standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **$3,000 \mu\text{g}/\text{m}^3$ to $30,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for methylethyl ketone based on the adverse health effects of this compound.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard

will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.

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5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE *Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- "*Framework for the Application of Socio-economic Analyses in Setting Environmental Standards.*" Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for MEK can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS# 78-93-3)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The Reference concentration (RfC) for inhalation exposure is 1 mg/m³ (1,000 µg/m³).

No carcinogenic unit risk values are reported for inhalation exposure. No ambient air exposure limits are defined.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System Database. United States Environmental Protection Agency, Washington DC.

Key Reference(s).

Mast, T.J., J.A. Dill, J.J. Evanoff, R.L. Rommereim, R.J. Weigel and R.B. Westerberg, 1989. Inhalation developmental toxicology studies: Teratology study of methyleneethyl ketone in mice. Final Report. Prepared by Pacific Northwest Laboratory, Battelle Memorial Institute, for the National Toxicology Program, Washington, DC. PNL-6833 UC-408.

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6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

No air quality guideline currently exists.

8. Key Risk Assessment Considerations:

The calculated RfC of 1 mg/m^3 for MEK represents an estimate of a long-term daily inhalation exposure of the human population that is not likely to cause adverse effects to the respiratory system nor adverse effects systemically. The derivation of the RfC considers developmental effects based on an inhalation study conducted on mice and reported in different formats by Schwetz *et al.* (1991) and Mast *et al.* (1989). Both a no-observed-adverse-effect-level (NOAEL) and a lowest-observed-adverse-effect-level (LOAEL) were identified.

Groups of 23 to 28 pregnant Swiss mice were exposed to MEK vapours at concentrations of 0, 398, 1,010, or 3,020 ppm for 7 hours/day during days 6 to 15 of gestation (Schwetz *et al.*, 1991). Dams were killed on gestational day 18 and although a concentration-related increase in relative liver and kidney weight was observed, the difference was statistically significant only at the highest dose level (US EPA, 1997). Neither maternal nor developmental toxicity was exhibited at 1,010 ppm or less. At the highest dose group (3,020 ppm), some mild maternal and developmental effects were observed (LOAEL). A mild decrease in mean fetal body weight was observed but it was statistically significant only in male fetuses at the highest dose group. There was a dose-related increase in the incidence of misaligned sternebrae in the fetuses but was statistically significant at the highest exposure concentration. No significant increase in any single malformation was found. However, some malformations such as cleft palate, fused ribs, missing vertebrae and syndactyly, were observed in one litter of the exposed group.

The US EPA used extrapolation factors to adjust from animal exposure levels to human exposure levels and applied uncertainty factors to protect sensitive individuals in the population. The level of 1,010 ppm was converted to a human equivalent dose of $2,980 \text{ mg/m}^3$ by assuming conditions of 25°C and 760 mm Hg, and adjusting for gas:extrarrespiratory effects (default value of 1.0 was used for the adjustment ratio, since values required for assessment were unknown for the experimental animal species). No adjustment was made for duration of exposure (US EPA, 1997).

The following uncertainty factors (UF) were applied to account for interspecies extrapolation (UF=10), sensitive individuals (UF=10), and incomplete database including a lack of chronic and reproductive toxicity studies (UF=10). An additional modifying factor of 3 was applied to address the lack of unequivocal data for respiratory tract effects. The overall factor applied to the NOAEL was 3,000 (US EPA, 1997).

The US EPA identifies concerns that insufficient data are presented for possible respiratory effects, despite corroborative principal and supporting studies for a developmental toxicity endpoint. Furthermore, no multi-generational studies were performed and only a single subchronic study was identified. None of the studies reviewed addressed the potential for MEK to cause irritant effects to the upper respiratory tract and nasal regions at short-term, elevated concentrations above the LOAEL.

Confidence in the principal study is medium, while confidence in the database and RfC are low (US EPA, 1997). The US EPA last reviewed the RfC for MEK in July of 1992.

9. *Key Risk Management Considerations:*

The RfC is designed to provide protection to the human population, including sensitive individuals exposed continuously over a lifetime.

10. *Multimedia Considerations of Guidelines:*

No guideline exists. The RfC only considers inhalation exposure from air sources.

11. *Other Relevant Factors:*

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS # 78-93-3)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for MEK. No risk-based concentration limit has been established for MEK. In 1997, the Office of Environmental Health Hazard Assessment proposed to adopt The US Environmental Protection Agency Reference Concentration (RfC) of 1,000 $\mu\text{g}/\text{m}^3$ as Chronic Reference Exposure Level (REL). In 1998, an Acute (one hour) REL of 26,000 $\mu\text{g}/\text{m}^3$ was proposed.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. *Documentation Available:*

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 645-647.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California.

OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Methyl Ethyl Ketone. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California.

6. Peer-Review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification list is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS, etc.) and additional widely recognized reference texts.

The RfCs, reference exposure levels (RELs) and cancer potency values reported in both the Draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritization of the areas and facilities for which risk assessments are required.

7. Status of Guideline:

Not applicable

8. Key Risk Assessment Considerations:

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for MEK. The State understands and identifies that the US EPA has established a RfC of 1,000 $\mu\text{g}/\text{m}^3$ based on decreased fetal birth weights in mice (ARB, 1996). Though this is recognized by the State, MEK is not listed under

Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996). Therefore, the State does not apply the US EPA's RfC.

MEK is identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment" which is the State's next step in establishing a potential air quality guideline value (ARB, 1997). Recently, the state of California has proposed to adopt the RfC of 1,000 $\mu\text{g}/\text{m}^3$ from the US EPA for its chronic inhalation Reference Exposure Level (REL) (OEHHA, 1997).

California has proposed an acute (one-hour) REL of 26,000 $\mu\text{g}/\text{m}^3$ (OEHHA, 1998). This was derived from LOAEL observed among four volunteers exposed to an increasing concentration of MEK between 90-270 ppm or 260,000-780,000 $\mu\text{g}/\text{m}^3$ over two hours (Nakaaki 1974, as cited in OEHHA, 1998). The reviewers note that it is unclear if at the lowest concentration the only effect was odour perception. However, a mild irritation effect was noted at 780,000 $\mu\text{g}/\text{m}^3$ which was considered a LOAEL. In another study of volunteers exposed at 200 ppm (590,000 $\mu\text{g}/\text{m}^3$) no neurological or irritation effects were seen (Dick *et al.*, 1992 as cited in OEHHA, 1998). Uncertainty factors were applied to the LOAEL from the Nakaaki (1974) study: 3 to take into account the observation of a mild irritation effect, and 10 to account for variations in sensitivity in humans, for a total uncertainty factor of 30.

California has also derived a level protective against severe adverse effects of 88,000 $\mu\text{g}/\text{m}^3$ based on findings from three developmental studies. A level protective against life-threatening effects of 1,385,000 $\mu\text{g}/\text{m}^3$ was derived from an LC_{50} in rats.

9. *Key Risk Management Considerations:*
Not applicable

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). MEK is not one of these substances.

11. *Other Relevant Factors:*

MEK is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Methylethyl ketone (MEK) (CAS# 78-93-3)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) is $200 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. Allowable ambient limit (AAL) is $200 \mu\text{g}/\text{m}^3$ (annual average)². The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

²During the course of the review of the MDEP's methodology and AALs, an error was detected in the application of the non-threshold uncertainty factor for MEK. This discrepancy was reported to representatives of the MDEP and the AAL will be modified accordingly. The AAL of $200 \mu\text{g}/\text{m}^3$ cited in this summary incorporated this change and is the correct guideline.

Key Reference(s):

US EPA, 1994. Integrated Risk Information System Database. United States Environmental Protection Agency, Washington, DC.

6. Peer-Review Process and Public Consultation:

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline(s):

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of MEK, an IRIS RfC was reported for this chemical. The MDEP, after having reviewed the basis for the MEK RfC, has adopted the level of 1.0 mg/m³ (1,000 µg/m³) for use in the MDEP air guidelines. This level was considered the starting point for the TEL derivation and was divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure. The TEL was, therefore, calculated as 200 µg/m³.

Non-Threshold Effects

The MDEP reported that there was insufficient evidence to classify MEK's carcinogenic or mutagenic potential (MDEP, 1990). The non-threshold effect exposure limit (NTEL) was developed from the IRIS RfC (1,000 µg/m³) by using a Non-Threshold Effects Uncertainty Factor (NTEUF) of 1. No

adjustment was made for multimedia considerations. The resulting NTEL for MEK was calculated as 1,000 $\mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. The MDEP states that, in cases where the TEL equals the AAL, the TEL concentration and averaging time (24-hour average) should be used (MDEP, 1990). Since the TEL was lower, it was adopted as the AAL. The AAL for MEK is 200 $\mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not include consideration of technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

A factor of 20% was applied to the RfC used as the basis of the guideline to allow for contributions from environmental media sources of exposure other than air.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS #78-93-3)

2. *Agency:* State of Michigan, Department of Environmental Quality (DEQ)

3. *Guideline Value(s):*

The 24-hour Initial Threshold Screening Level (ITSL) is 1,000 $\mu\text{g}/\text{m}^3$.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that toxic from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each air toxic are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a toxic, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

Key Reference(s):

Schwetz, B.A., T.J. Mast, R.J. Weigel, J.A. Dill and R.E. Morrissey, 1991. Developmental toxicity of inhaled methylethyl ketone in Swiss mice. *Fund. Appl. Toxicol.* 16: 742-748.

Mast, T.J., J.A. Dill, J.J. Evanoff, R.L. Rommereim, R.J. Weigel and R.B. Westerberg, 1989. Inhalation developmental toxicology studies: Teratology study of methylethyl ketone in mice. Final Report. Prepared by Pacific Northwest Laboratory, Battelle Memorial Institute, for the National Toxicology Program, Washington D.C. PNL-6833 UC-408.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of this value. Specifically, information from the US EPA's process for development of reference concentrations (RfCs), upon which the ITSL for MEK is based, were employed.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The ITSL for MEK was adopted from the RfC developed by the US EPA. The ITSL, which is averaged over 24 hours, equals the inhalation RfC. (For detailed information on the derivation of the US EPA RfC, please see Section 5.1, Federal Government of the United States).

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Methyl ethyl ketone (MEK) (CAS # 78-93-3)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey has not identified a specific air concentration guideline value for MEK. A reference concentration (RfC) of 1,000 $\mu\text{g}/\text{m}^3$ based on decreased fetal birth weights in mice is recognised and applied for the purposes of conducting risk assessments under the Air Quality Permitting Program.

4. *Application:*

The NJDEP, Bureau of Air Quality Evaluation's Air Quality Permitting Program requires a proponent to complete a risk assessment in conjunction with applying for an air pollution control pre-construction permit. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act*. The RfC for MEK is identified for the purpose of completing such a risk assessment.

5. *Documentation Available:*

NJDEP, 1994. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. NJDEP, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The RfC referenced above should be used in the risk assessment to estimate the public health risks for inhalation of MEK using the following equation:

$$\text{Hazard Quotient} = C / \text{RfC}$$

where C = maximum ambient air concentration in $\mu\text{g}/\text{m}^3$

RfC = Inhalation RfC = 1,000 $\mu\text{g}/\text{m}^3$

This RfC is adopted from IRIS and is based on decreased fetal birth weights in mice. The maximum annual average ambient air concentrations of pollutants (C) are derived from one of three approaches: an initial risk screening assessment, dispersion modelling, or air monitoring programs (NJDEP, 1997). In the case of MEK, air monitoring programs have little information on its annual average concentrations (NJDEP, 1997).

Hazard indices which are less than or equal to one indicate a risk which is considered to be negligible. However, hazard indices which are greater than one represent risks which are of concern to the State, and will be evaluated and managed on a case-by-case basis.

9. Key Risk Management Considerations:

The RfC is not a guideline or standard for MEK. The State does, however, identify MEK as a Toxic Air Contaminant.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS# 78-93-3)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources

3. *Guideline Value(s):*

Short-term Guideline Concentration (SGC) is 140,000 $\mu\text{g}/\text{m}^3$ (1-hour average).

Annual Guideline Concentration (AGC)³ is 1,000 $\mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is primarily intended for use in the decision making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257) and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short-term and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision making process using scientific data and professional judgement, however, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources. Albany, New York.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices, Sixth Edition. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH.

US EPA, 1997. Integrated Risk Information System (IRIS) Database. United States Environmental Protection Agency. Washington, DC.

³During the course of the review of the New York State AGCs, an error was detected in the identification of the criterion for MEK. This discrepancy was reported to the state representative and will be corrected in their documentation. The AGC of 1,000 $\mu\text{g}/\text{m}^3$ cited here is correct (NYSDEC, 1997).

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgement was employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. Status of Guideline(s):

Current.

8. Key Risk Assessment Considerations:

MEK is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC was derived from the ACGIH Threshold-Limit-Value-Time-Weighted-Average (TLV-TWA) in 1991. The ACGIH TLV-TWA was adjusted to account for the differences in the application from an occupational limit (8 hours/day, 5 days/week occupational exposure) to an ambient limit (24 hours/day, 7 days/week). The factor used for the adjustment of the occupational limit of 590 mg/m³ MEK for the SGC was 4.2.

The AGC for MEK was adopted from the US EPA RfC.

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. Multimedia Considerations of Guidelines:

The NYSDEC guideline only considers human exposure to contaminants in the air.

11. Other Relevant Factors:

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* *Methylethyl ketone (MEK) (CAS # 78-93-3)*

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

None.

4. *Application:*

None.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*

Not applicable.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Methyl ethyl ketone (MEK) (CAS # 78-93-3)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

MEK is classified as a class 3 gaseous organic substance (gO.3). This classification imposes an emission standard of 150,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 3.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorized into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. *Peer-review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of $150 \mu\text{g}/\text{m}^3$ in the case of a mass flow of 3.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

9. *Key Risk Management Considerations:*

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS# 78-93-3)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No information available.

4. *Application:*

No information available.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. Chemosphere 27(9) 1691-1706.

6. *Peer-review Process and Public Consultation:*

No information available.

7. *Status of Guideline:*

No information available.

8. *Key Risk Assessment Considerations:*

No information available.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

No information available.

11.10 Agency Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Methyleneethyl ketone (MEK) (CAS # 78-93-3)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

No guideline has been established. MEK has not been assessed or evaluated under first Priority Substance List (PSL1) and is not listed for evaluation under PSL2.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, PSL2 Secretariat, October 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	Either ' <i>Reference Exposure Level</i> ' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or ' <i>Recommended Exposure Limit</i> ' used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
METHYLISOBUTYL KETONE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Methylisobutyl ketone was identified as a priority compound for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing guideline in 1975. A review of the scientific and technical information relevant to setting an ambient air quality standard for methylisobutyl ketone has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for methylisobutyl ketone.

Methylisobutyl ketone (MIBK; CAS# 108-10-1) is a colourless, flammable substance with a fruity, ethereal odour. It has an odour detection threshold that ranges from 400 - 32000 $\mu\text{g}/\text{m}^3$. It is primarily used as a solvent in protective coatings and chemical synthesis. MIBK is also used as a process solvent to separate and purify various substances including: organic and inorganic chemicals, certain metal ions, antibiotics, and other pharmaceuticals.

Data from the Canadian National Pollutant Release Inventory (NPRI) indicate that MIBK was released almost exclusively to the atmosphere in Canada and in Ontario. Furthermore, the quantities released between 1993 and 1997 were consistent. Approximately 90% of the total atmospheric releases in Canada occurred in Ontario.

Environment Canada has collected ambient air data for MIBK from January 1993 to December 1995 from nine monitoring stations in cities across Canada. A mean concentration of 0.24 $\mu\text{g}/\text{m}^3$ was detected; measured concentrations ranged from a minimum of no detection (detection limit of 0.1 $\mu\text{g}/\text{m}^3$) to a maximum of 2.95 $\mu\text{g}/\text{m}^3$ in Windsor, Ontario.

Methylisobutyl ketone is primarily absorbed through the lungs, although gastrointestinal and dermal absorption can also occur. The respiratory and nervous systems, eyes, and skin can be affected by exposure to MIBK. Inhalation of MIBK vapour may cause depression of the central nervous system (CNS), dizziness, nausea, confusion, or collapse. Dermal contact may cause dermatitis. Chronic or repeated exposure to relatively high concentrations of MIBK may result in toxic effects to the CNS, gastrointestinal tract, liver, and kidneys.

The current 24-hour Ambient Air Quality Criterion (AAQC) and the half-hour Point of Impingement (POI) guidelines are both set at 1,200 $\mu\text{g}/\text{m}^3$, which is based on the odour effect of MIBK.

In revising the air quality standards of Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Of the criteria reviewed, the Ministry has evaluated and agreed with the states of Massachusetts, Michigan, and New York and accepted the scientific studies which support the development of the occupational exposure limit of 205,000 $\mu\text{g}/\text{m}^3$ from the American Conference of Governmental Industrial Hygienists (Threshold Limit Value-Time-weighted Average) and the National Institute for Occupational Safety & Health (Recommended Exposure Limit). Applying an exposure time conversion factor and appropriate uncertainty factors to the occupational exposure limit could result in a 24-hour criterion of 1,366 $\mu\text{g}/\text{m}^3$ which is in close agreement with the current odour-based 24-hour AAQC. Deriving a 24-hour AAQC from TLV-TWA will result in a criterion higher than the current Ontario odour-based 24-hour AAQC. Therefore, replacing the odour-based POI and 24-hour AAQC of 1,200 $\mu\text{g}/\text{m}^3$ is not recommended.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, the odour property of this compound, and comments received from stakeholders, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for methylisobutyl ketone:

- **a 24-hour average AAQC of 1,200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for MIBK, based on the odour nuisance, the adverse health effects and the potential interaction with other hydrocarbon solvents of this compound; and,**
- **a half-hour average POI of 1,200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for MIBK, based on the odour nuisance of this compound. This odour based POI is also protective of health.**

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Methylisobutyl ketone was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing guideline in 1975. A review of scientific and technical information relevant to setting an ambient air quality standard for methylisobutyl ketone had been provided in a previous document, and was distributed to stakeholders for their comments. This document therefore provides the rationale for recommending an AAQC and a POI standard for methylisobutyl ketone.

2.0 General Information

2.1 Physical and Chemical Properties

The following list provides some general information on methylisobutyl ketone and its properties:

CAS #	108-10-1
RTECS #	SA9275000
UN #	1245
Formula	C ₆ H ₁₂ O
Molecular Weight	100.18 g/mol
Boiling Point	117-118°C
Flash Point	23°C
Vapour Density (air = 1)	3.45
Vapour Pressure	16 mm Hg @ 20°, 19.86 mm Hg @ 25°C
Log Octanol/Water Partition Coefficient	Log K _{ow} = 1.09; 1.19 (estimated)
Henry's Law Constant	1.38 x 10 ⁻⁴ atm m ³ /mol @ 25°C
Conversion Factors	1 ppm = 4.10 mg/m ³ 1 mg/m ³ = 0.24 ppm
Solubility	17,000 mg/L @ 20°C; 19,000 mg/L @ 25°C
Common Synonyms	Hexone, 4-methyl-2-pentanone, MIBK, MIK, isopropylacetone

Methylisobutyl ketone is a colourless, flammable liquid (US EPA, 1994) with a fruity, ethereal odour (Lewis, 1992). The odour thresholds have been reported to be between 0.3 and 0.7 ppm (1,230 to 2,870 µg/m³) (ACGIH, 1991) or 0.1 to 7.8 ppm (400 to 32,000 µg/m³) with a geometric mean of 0.88 ppm (3,600 µg/m³) (AIHA, 1989). Using an Odour Impact model analysis based on the odour effects of MIBK sensed by panel members, the 50% detection level was found to be 6,300 µg/m³ (Nagy, 1991)

2.2 Uses for MIBK

Methylisobutyl ketone has several industrial applications. It is primarily used as a solvent in protective coatings and chemical synthesis. It is also used as a process solvent to separate and purify various substances, including organic and inorganic chemicals, certain metal ions, antibiotics, and other pharmaceuticals. MIBK is used in purifying stearic acid and extracting rosin from softwood,

particularly pine. It is added to adhesives, printing ink, and special lubricating oils and is used by manufacturers of pesticides, textiles, and leather (HSDB, 1997; US EPA, 1994).

2.3 Sources and Levels

Sources

Methylisobutyl ketone occurs naturally in certain foods and beverages, and has also been found in flavouring agents. Industrial and domestic uses result in the greatest releases to the environment, particularly from its use as a solvent in paints, lacquers, varnishes, and adhesives (US EPA, 1994).

Environment Canada's National Pollutant Release Inventory (NPRI) summarises the emissions of chemicals in Canada based on information provided by reporting facilities (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996; NPRI, 1997). Data obtained from the NPRI reports from 1993 to 1997 indicate that there were about 60 to 70 sources of MIBK emission in Canada, of which more than 65% were in Ontario. The annual atmospheric releases of this compound were 782, 746, 721, 754 and 727 tonnes in the reporting years of 1993, 1994, 1995, 1996 and 1997, respectively. Releases of MIBK are consistent within these 5 reporting years. Atmospheric emissions of MIBK in Ontario showed a similar pattern. There were 696, 630, 640, 680 and 663 tonnes of MIBK released to the atmosphere in Ontario during 1993, 1994, 1995, 1996 and 1997, respectively. Ontario emissions constituted approximately up to 90% of the national atmospheric releases. The release data of 1997 indicated that atmospheric releases accounted for more than 99% of the total MIBK releases in Ontario, as well as nation-wide. Most of the releases in these years were attributed to industries of petroleum refinery, rubber, plastic, paper and allied products, wall covering, textile products, wood and chemical products, furniture and fixture, automotive and parts industries.

Ambient Air Concentrations

Environment Canada has collected ambient air data for MIBK for January 1993 to December 1995 from nine monitoring stations in cities across Canada. A mean concentration of $0.24 \mu\text{g}/\text{m}^3$ was detected; measured concentrations ranged from a minimum of no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $2.95 \mu\text{g}/\text{m}^3$ in Windsor, Ontario (Environment Canada, 1997). Monitoring of MIBK by the MOE indicated that half-hour average concentrations of MIBK in Ontario ranged from 8 to $80 \mu\text{g}/\text{m}^3$. (MOEE, 1997). Maximum levels were detected at an automotive painting plant in Oakville in 1991 ($80 \mu\text{g}/\text{m}^3$) and a kitchen cabinets manufacturing facility in the Greater Toronto Area in 1994 ($59 \mu\text{g}/\text{m}^3$) (MOEE, 1997).

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 72 facilities with emissions of MIBK covered by a Certificate were identified. These approvals were for emissions

from industries in automotive spray paint and parts, adhesives, plastic and metal products. The median Ground Level Concentration estimated by Regulation 346 dispersion modelling for all 72 sources was approximately $36 \mu\text{g}/\text{m}^3$. The minimum and maximum were 0.001 and $517.2 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

Ninety-nine percent of direct environmental releases of MIBK are to air (NPRI, 1996). Methylisobutyl ketone is volatile and evaporates readily. The primary degradation pathway for MIBK in the atmosphere, with a half-life of 16 to 17 hours, is the reaction with photochemically produced hydroxyl radicals (US EPA, 1994). Direct photolysis of MIBK is also expected to occur in the atmosphere with a half-life of 15 hours, producing acetone (US EPA, 1994).

Methylisobutyl ketone is unlikely to adsorb to organic soils due to its low soil absorption coefficient ($K_{oc} = 123$) and moderate water solubility. Methylisobutyl ketone is mobile and may leach into groundwater; it has also been detected in landfill leachate (HSDB, 1997). Soil and water microorganisms contribute to the degradation of MIBK. Plants and animals are unlikely to accumulate MIBK, due to its low octanol-water partitioning coefficient ($\log K_{ow} = 1.09$) and moderate water solubility (HSDB, 1997).

3.0 Toxicology of Methylisobutyl Ketone

The following toxicological review of MIBK is primarily focussed on the inhalation route of exposure since this pathway appears to be the major route of intake in humans and most (greater than 99%) of the released MIBK was emitted to the air (NPRI, 1996). Data on other exposure media are included where relevant or where inhalation data are lacking.

Methylisobutyl ketone is absorbed primarily through the lungs by the inhalation route of exposure, although absorption through the gastrointestinal tract (GIT) by ingestion and by the skin through dermal contact can also occur. Once absorbed, MIBK may distribute extensively into the brain, liver, lung, vitreous fluid, and kidneys. In guinea pigs, intraperitoneally delivered MIBK was shown to be oxidized to a major metabolite, 4-hydroxy-4-methyl-2-pentanone (HMP), and to be reduced to a minor metabolite, 4-methyl-2-pentanol (4-MPOL), which was conjugated with sulphate or glucuronic acid and excreted in urine (WHO, 1990; US EPA, 1994). Inhaled MIBK is also rapidly eliminated in expired air, although small amounts of the parent compound are also excreted in the urine. Less than 0.1% of unmetabolized MIBK was found in the urine of humans within the first three hours after exposure (US EPA, 1994).

3.1 Acute Toxicity

The respiratory and nervous systems, eyes, and skin can be affected by exposure to MIBK. Inhalation of MIBK vapour may cause central nervous system (CNS) depression, dizziness, nausea, confusion, or collapse, while dermal contact may cause dermatitis (ACGIH, 1991; US EPA, 1994). Among occupationally exposed workers and exposed volunteers, a concentration of 410 mg/m³ (based on an 8-hour breathing rate) caused headaches, nausea, and irritation of the respiratory tract (WHO, 1990). In an experiment with human volunteers, a 2-hour exposure to MIBK (10, 100 and 200 mg/m³ or 2.4, 24.4, and 48.8 ppm) induced CNS symptoms such as headache and /or vertigo and/or nausea (Hjelm *et al.*, 1990 as cited in WHO, 1990).

The acute toxicity of MIBK to animals is relatively low through the inhalation route of exposure. Total lethality was observed in rats treated with 4,000 ppm (16,400 mg/m³) MIBK for 4 hours; no lethality was found in animals treated with 2,000 ppm (8,200 mg/m³) (as reviewed in WHO, 1990). The adverse effect of inhaled MIBK was studied in guinea pigs. Female guinea pigs were exposed to MIBK at 1000, 16,800 and 28,000 ppm (4,100, 69,000, 115,000 mg/m³, respectively) for up to 24 hours. There was minimal eye or nasal irritation at 4,100 mg/m³. The two higher concentrations produced noticeable irritation of the eyes and the nose, followed by salivation, lacrimation, ataxia, progressive narcosis and death. The highest concentration caused death to 50% of the animals within 45 minutes of exposure. Histopathological examinations indicated fatty livers and congestion of the brain, lungs and the spleen, but no damage to the heart and kidneys (as reviewed in WHO, 1990).

3.2 Subchronic and Chronic Toxicity

Chronic, or repeated exposure to relatively high concentrations of MIBK may result in toxic effects to the CNS, GIT, liver, and kidneys. Nausea, headache, burning eyes, weakness, somnolence, insomnia, and intestinal pain were reported by workers exposed to 2,050 mg/m³ MIBK for 20-30 minutes/day, and to 328 mg/m³ for the remainder of the workday. Even at 410 mg/m³ for the short exposure and 205 mg/m³ for the duration of the day, some workers experienced eye irritation, GIT and neurological problems such as loss of appetite, stomach ache, headache, nausea, vomiting, insomnia, somnolence and some unsteadiness. Slight liver enlargement was found in some individuals at both concentrations (as reviewed in ACGIH, 1991; US EPA, 1994; WHO, 1990).

Rats exposed to 100 ppm (410 mg/m³) for 2 weeks resulted in an increase in kidney weight. At 200 ppm (820 mg/m³) for two weeks or at 410 mg/m³ for 90 days, an increase in both the liver and kidney weights was observed. Histological examination showed hyaline droplets in the proximal tubules of the kidney. Rats, dogs and monkeys were exposed to MIBK at 410 mg/m³ (100 ppm) under reduced oxygen tension and atmospheric pressure (65% oxygen and 34.7 kPa) for 90 days, which resulted in increases in liver and kidney weights. Hyaline droplets were noticed in the kidney epithelium of the rats

which disappeared after a recovery period of 3 to 4 weeks. No histological changes were observed in dogs or monkeys (as reviewed in WHO, 1990).

Four groups of F-344 rats (6 per sex) and B6C3F₁ mice (6 per sex) were exposed to MIBK at 0, 41, 2,050 and 8,180 mg/m³ (0, 10, 501 and 1996 ppm, respectively) for 6 hours/day for 5 days (with 2 days off followed by 4 more consecutive days of exposure). At the highest dose group, lacrimation with no ophthalmological changes, was observed and no weight gain was noticed in all animals. Liver weight was increased - relative to body weight - in both sexes of rats and in female mice at the highest concentration. A statistically significant increase in liver weight was observed in male rats at the 2,050 mg/m³ concentration. At 8,180 mg/m³, both male and female rats and female mice showed a significant increase in absolute and relative kidney weight; however, a significant decrease in relative kidney weight in the male mice was observed. Among the animals tested at the 2,050 mg/m³ concentration, only the male mice had a noticeable increase in kidney weight. Histologically, hyaline droplets were observed in the kidneys of the male rats exposed to 2,050 and 8,180 mg/m³ and epithelial regeneration of the proximal convoluted tubules was seen at 8,180 mg/m³. No histological changes were observed in rats and mice exposed to 41 mg/m³ and this concentration was considered the no-observed-adverse-effect-level.

In a later study, four groups of fourteen F-344 rats and B6C3F₁ mice, of both sexes were exposed to MIBK at 0, 50, 250 or 1000 ppm (0, 205, 1,025 or 4,100 mg/m³, respectively) for 6 hours/day, 5 days/week for 90 days. Growth retardation and clinical effects were apparent in both rats and mice. In addition to body and organ weight measurements, clinical observations were made. Haematology, ophthalmology, gross pathology and histology were also examined. In rats, water consumption, urine and serum chemistry were performed. At 4,100 mg/m³, male rats and mice demonstrated a slight increase in liver weight and in liver weight per body weight ratio; a slight increase in liver weight was also observed in male mice exposed to 1,025 mg/m³. There were no gross or microscopic hepatic lesions, and no changes in urine and serum chemistry. There was an increase in the number of hyaline droplets in the proximal tubular cells of the kidney in the male mice exposed to 1,025 to 4,100 mg/m³. No other gross or microscopic changes in the kidneys were observed. The effect of hyaline droplet increase by MIBK was considered specific to male rats because of the presence of alpha-2μ-globulin (as reviewed in WHO, 1990).

3.3 Developmental and Reproductive Toxicity

There are insufficient data to assess the adverse developmental/reproductive effects of MIBK in humans (Calabrese and Kenyon, 1991; US EPA, 1994). Developmental toxicity was seen in rats and mice exposed to MIBK by inhalation (US EPA, 1994). Thirty five pregnant Fischer 344 rats and 30 pregnant CD-1 mice were exposed to MIBK at 300, 1000 and 3000 ppm (1,230, 4,100 and 12,300 mg/m³) on days 6 - 15 of gestation (as reviewed in WHO, 1990). Rats were sacrificed on day 21

whereas mice were sacrificed on day 18. The fetuses were examined for external, visceral and skeletal changes. At the concentration of 12,300 mg/m³, MIBK was fetotoxic in rats (reduced fetal body weight per litter and delays in skeletal ossification). However, this concentration induced maternal toxic effects such as decreased body weight, increased relative kidney weight gain and decreased food consumption. Clinical observations in parental rats included loss of coordination, negative toe pinch, muscular weakness, piloerection, lacrimation, and perioral encrustation. No increase in fetal malformation was noticed in any test group. At the two lower concentrations (1,230 and 4,100 mg/m³), no maternal, embryo, fetotoxicity or malformation were apparent.

No reproductive organ toxicity was reported in a 2-week probe and a 14-week subchronic inhalation study (MIBK concentrations not noted) in Fischer 344 rats and B6C3F₁ mice (as reviewed in US EPA, 1994).

3.4 Genotoxicity

Evidence suggests that MIBK is unlikely to be genotoxic in mammalian systems (HSDB, 1997). MIBK tested positive in the mouse lymphoma and cell transformation assays, and negative in Ames tests and the mouse micronucleus test (US EPA, 1994). Results for unscheduled DNA synthesis were also negative (HSDB, 1997). MIBK was not mutagenic in *E. coli* tester strains WP2 and WP2uvrA or in *S. cerevisiae* tester strain JD1, with or without metabolic activation (US EPA, 1994).

3.5 Carcinogenicity

No data were found on the carcinogenicity of MIBK in humans or animals (ACGIH, 1991; Calabrese and Kenyon, 1991; HSDB, 1997; US EPA, 1994). MIBK has not been evaluated by the United States Environmental Protection Agency for evidence of human carcinogenic potential (US EPA, 1997).

3.6 Methylisobutyl Ketone in Solvent Mixtures

The neurotoxic effects of *n*-hexane were suggested to be potentiated by MIBK. Data are limited concerning the potentiation of the neurotoxic effects of *n*-hexane and haloalkane solvents by MIBK, as compared with the more well-examined potentiation of the neuropathological effects of *n*-hexane and other haloalkane solvents by methylethyl ketone (as reviewed in WHO, 1993). The possible interaction of MIBK with other simultaneously exposed hexacarbon or haloalkane solvents warrants additional consideration.

Studies concerning this effect of MIBK in humans are insufficient. There was only one incidence of polyneuropathy reported in a case of chronic solvent mixture abuse; the mixture contained methylethyl

ketone, MIBK and many other solvents (no *n*-hexane or methylbutyl ketone). In an animal study, MIBK, *n*-hexane and MIBK/*n*-hexane mixtures were given to hens (five per group) by inhalation continuously for 90 days, followed by a 30-day observation period (as reviewed in WHO, 1990). One group received MIBK at 1000 ppm (4,100 mg/m³), another group was exposed to 1000 ppm (3,520 mg/m³) *n*-hexane and other groups were exposed simultaneously to *n*-hexane at 3520 mg/m³ and MIBK at 100, 250, 500 or 1000 ppm (410, 1,025, 2,050 or 4,100 mg/m³). Control hens were exposed to ambient air only in a test chamber. Hens exposed to MIBK at 4,100 mg/m³ showed weakness of the legs with subsequent recovery. *n*-Hexane at 3,520 mg/m³ produced mild ataxia. Simultaneous exposure to 3,520 mg/m³ *n*-hexane and 1,025, 2,050 or 4,100 mg/m³ MIBK demonstrated signs of neurotoxicity including paralysis and the severity was dose-related to MIBK concentrations. Hens exposed to 3,520 mg/m³ *n*-hexane and 410 mg/m³ MIBK together developed severe ataxia throughout the observation period. Histopathological examination of hens exposed to *n*-hexane/MIBK mixture indicated large swollen axons and degeneration of the axon, myelin of the spinal cord and peripheral nerves. Hens exposed to MIBK only, did not show histopathological abnormalities of the central nervous system. Data from a subsequent experiment with hens exposed to 3,520 mg/m³ *n*-hexane and 4,100 mg/m³ MIBK for 50 days suggested that MIBK magnified the neurotoxicity of *n*-hexane by the induction of liver microsomal oxidative enzyme, cytochrome P-450, resulting in the formation of the potent neurotoxic metabolites of *n*-hexane.

MIBK was shown to increase the neurotoxicity of *n*-hexane (species not specified), possibly related to its ability to induce liver microsomal cytochrome P-450, which increased activation of *n*-hexane to the potent neurotoxic metabolites (as reviewed in HSDB, 1997). MIBK was shown to potentiate the haloalkane carbon tetrachloride (CCl₄) hepatotoxicity in male Sprague-Dawley rats. Animals were orally treated with MIBK prior to the intraperitoneal injection of CCl₄ at doses of 0 to 0.5 mL/kg. Plasma alanine-aminotransferase activity and bilirubin concentrations were monitored to assess liver injury following the CCl₄ treatment. Results revealed that increasing the CCl₄ dosage from 0.01 to 0.10 mL/kg decreased the minimum effective dosage of MIBK ten-fold (as reviewed in HSDB, 1997).

3.7 Environmental Effects

There are no data on the effects of MIBK exposure to terrestrial wildlife. Acute toxicity values for fish range from 460 mg/L (24-h LC₅₀) for goldfish (*Carassius auratus*) to 744 mg/L (48-h LC₅₀) for golden orfe (*Leuciscus idus melanotus*) (WHO, 1990). Aquatic invertebrates are less sensitive to MIBK than fish with 24-hour LC₅₀ values ranging from 1,230 mg/L to 4,280 mg/L for brine shrimp (*Artemia salina*) and water flea (*Daphnia magna*), respectively (WHO, 1990). A threshold concentration for the reduction of total biomass in green algae was observed at 136 mg/L after an 8-day exposure period (Bringmann et al, 1977). The relatively high volatility, rapid atmospheric transformation, and biodegradability of MIBK indicate that adverse environmental effects are only likely to occur after a spill or from uncontrolled industrial effluents (WHO, 1990).

4.0 Existing Air Quality Criteria

4.1 Overview

The current Ontario half-hour POI guideline and the 24-hour AAQC for MIBK are both set at 1,200 $\mu\text{g}/\text{m}^3$, which is based on the odour effect of this compound.

The documentation for ten agencies (the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government) was reviewed for the existence and basis of air quality criteria for MIBK. A brief summary of this review is presented in Table 1 and agency-specific summaries of information concerning air quality guidelines for MIBK are presented in Section 11f.0 of the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE typically uses a factor of 15 to convert from guidelines based on annual average concentrations to half-hour point-of-impingement limits, and a factor of 3 to convert from guidelines based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality guidelines based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Since no data has been found on the carcinogenicity of MIBK, it is not possible to consider this endpoint in the development of air quality criteria. Of the agencies reviewed, five of them, the Commonwealth of Massachusetts, the States of Michigan, New Jersey and New York, and The Netherlands, have developed reference values or criteria for MIBK. The air quality guidelines for MIBK are derived from the ACGIH's TLV-TWA limit or the REL from NIOSH (NIOSH, 1988) for MIBK of 50 ppm (205,000 $\mu\text{g}/\text{m}^3$). Annual average criteria range from 55.7 to 480 $\mu\text{g}/\text{m}^3$ and short-term criteria (24 hour or less) range from 55.7 to 48,000 $\mu\text{g}/\text{m}^3$. These differences are due to variations in policy, with regards to the margin of safety in the derivation of ambient air criteria from recommended occupational levels.

Table 1. Summary of Existing Air Quality Guidelines⁽¹⁾ for MIBK

Agency	Guideline Value	Basis of Guideline	Date ⁽²⁾	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration): under review.		1997	
California	None.			MIBK appears on the Toxic Air Contaminants Identification List, but has yet to undergo a needs assessment.
Massachusetts	TEL (Threshold Effects Exposure Limits): 55.7 µg/m ³ (24-hour average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 55.7 µg/m ³ (annual average).	TLV-TWA from ACGIH.	1997	
Michigan	ITSL (Initial Threshold Screening Level): 2,050 µg/m ³ (8-hour average).	TLV-TWA from ACGIH.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC: 80 µg/m ³ (annual average).	RfC from US EPA's Health Effects Assessment Summary Table (HEAST).	1994	Permitting application. The RfC must be used in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): 48,000 µg/m ³ (1-hour average).	Recommended Exposure Limit (REL)-TWA from NIOSH.	1997	Used for permitting.
	AGC (Annual Guideline Concentration): 480 µg/m ³ .	REL-TWA from NIOSH.	1997	Used for permitting.
WHO	None.			
Netherlands	150,000 µg/m ³ (half-hour average).	Emission standard.	1992	Used for permitting.
Sweden	None.			
CEPA	None.			
Ontario	half-hour POI guideline: 1,200 µg/m ³ .	Both the POI and AAQC are based on odour.	1975	
	24-hour AAQC: 1,200 µg/m ³ .			

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.

Massachusetts based its Threshold Effects Exposure Limit (TEL) and Allowable Ambient Limit (AAL) on the Threshold Limit Value-Time Weighted Average (TLV-TWA) of the American Conference of Governmental Industrial Hygienists (ACGIH). Michigan based its Initial Threshold Screening Level (ITSL) on the ACGIH's TLV-TWA, also. New Jersey based its Reference Concentration (RfC) on the United States Environmental Protection Agency's (US EPA) RfC listed in their Health Effects Assessment Summary Table (HEAST). However, the US EPA withdrew its RfC, pending further review for this reference value. New York based its Short-term Guideline Concentration (SGC) and Annual Guideline Concentration (AGC) on the Recommended Exposure Limit (REL) from the National Institute of Occupational Health and Safety (NIOSH). Of the guidelines reviewed, the Massachusetts Department of Environmental Protection (MDEP) considers inhalation as one of the intake routes of multimedia exposure (MDEP, 1994).

The Netherlands set an emission standard of $150,000 \mu\text{g}/\text{m}^3$ for MIBK for the purpose of permitting. The scientific basis for the derivation of this guideline was not available. None of the following agencies have set air guidelines for MIBK: the State of California, the WHO, Sweden or the Canadian Federal Government.

4.2 Evaluation of Existing Criteria

The RfC of the US EPA for MIBK has been withdrawn pending review. In the absence of this reference criterion, most state agencies have derived their air quality guidelines from the occupational exposure limit values.

The ACGIH reported that the highest concentration of MIBK that most human subjects found satisfactory for 8 hours, of continuous exposure was 100 ppm ($410 \text{ mg}/\text{m}^3$) (ACGIH, 1991). Irritation of the eyes, nose, and throat was reported in most of the members of a 19-person workforce, exposed at 80 to 500 ppm (328 to $2,050 \text{ mg}/\text{m}^3$) MIBK for 20 to 30 minutes daily during an 8-hour work shift (ACGIH, 1991). More than half of the workers also complained of weakness, loss of appetite, headache, burning in the eyes, stomach ache, nausea and vomiting. Based on the findings of several studies in humans, the ACGIH considers that the TLV-TWA of 50 ppm should adequately protect workers from the potential irritant effects, neurasthenic symptoms (functional fatigue or weakness) and other systemic toxicities (including liver and kidney pathology) associated with exposure to MIBK greater than 50 ppm ($205,000 \mu\text{g}/\text{m}^3$) (ACGIH, 1991).

However, adverse effects have been noted in animal and human studies at the recommended occupational exposure limit. ACGIH (1991) reports adverse effects in baboons at the TLV-TWA level of 50 ppm. An impairment on accuracy of performance of tasks in a delayed match-to-sample discrimination test was noted in baboons exposed to 50 ppm MIBK for 7 days. A follow-up study in the 19-person workplace, which was conducted five years after the original study described above,

identified air concentrations ranging from 50 to 105 ppm MIBK. One of the original workers reported eye irritation at these levels and a few workers still complained of gastrointestinal and CNS disturbances (ACGIH, 1991).

Annual average criteria range from 55.7 to 480 $\mu\text{g}/\text{m}^3$. For MIBK, Massachusetts uses its 24-hour criterion for its allowable ambient level. New York divided the occupational level by a factor of 420, i.e. 4.2 to adjust for continuous exposure and 100 for contaminants considered as having moderate toxicity. New Jersey adopted the US EPA's RfC of 80 $\mu\text{g}/\text{m}^3$ from the 1993 Health Effects Assessment Summary Table (HEAST). HEAST is a summary of the health effects levels, including RfCs derived by the US EPA (1993). The state of New Jersey has not adjusted their RfC in light of the ongoing review carried out by the US EPA (NJDEP, 1997b).

Short-term criteria (24 hour or less) range from 55.7 to 48,000 $\mu\text{g}/\text{m}^3$. Massachusetts divided the occupational health limit by a factor of 3675: 4.2 to account for continuous exposure, 1.75 for differences in sensitivity between adults and children, 10 for sensitive populations, 10 for incomplete toxicological data, 5 for exposure routes other than inhalation. Michigan used a factor of 100 to derive its Initial Threshold Screening Level and New York divided the occupational limit by 4.2 to convert from an eight hour work day to a continuous exposure.

From the review of uses and release patterns of MIBK in Canada and particularly in Ontario, which indicates that most of the MIBK emitted is released to the atmosphere (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996). Together with data based on the physico-chemical properties of MIBK and the environmental partition modelling, it would appear that the inhalation route of exposure is the major, if not the only, intake pathway of concern for human health. This would indicate that there is no need to incorporate multi-media considerations when deriving air quality standards for MIBK in Ontario.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including methylisobutyl ketone, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and technical or economic impacts that may be anticipated as a consequence of revision of the air quality standards.

During the consultation period the Ministry received three submissions from various stakeholders regarding the draft document for methylisobutyl ketone. A stakeholder in the automotive manufacturing

industry indicated that the current odour-based POI would provide a sufficient margin of safety over the health-based toxicity thresholds and therefore recommended that the Ministry maintain the current POI standard for MIBK. One automotive equipment and parts manufacturer replied with a similar suggestion. Stakeholders in the petroleum products industry indicated that a full risk management process would be required if the Ministry intended to reduce the current air quality standard substantially.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed ambient air quality criteria and POI standard which are presented in Section 8.0 below. This step represents the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for methylisobutyl ketone.

7.0 Considerations in the Development of Air Quality Standards for methylisobutyl ketone

The current 24-hour Ambient Air Quality Criterion and the half-hour point of impingement guideline are both set at $1,200 \mu\text{g}/\text{m}^3$, which is based on the odour effect of MIBK.

The limited human and animal data on the toxicology of MIBK suggests that the primary health concern is its neurological effects on the central nervous system. Brief exposures of humans to MIBK at $10,000 - 410,000 \mu\text{g}/\text{m}^3$ can result in eye irritation, headaches, nausea, dizziness, and fatigue. Chronic occupational exposure to relatively high concentrations ($2,050,000 \mu\text{g}/\text{m}^3$) of MIBK may have toxic effects on the central nervous system (headaches and dizziness), gastrointestinal upset and weight changes in the livers and kidneys. In the absence of an inhalation reference concentration from the US EPA, most of the U.S. state agencies have derived their air quality criteria based on the occupational exposure limits of $205,000 \mu\text{g}/\text{m}^3$ (50 ppm) from either the ACGIH or the NIOSH.

When using occupational health levels to derive their ambient air criteria, various US jurisdictions use standard conversion factors. However, a few reports have indicated that inhalation exposure to MIBK

at the occupational exposure limit has resulted in some mild gastrointestinal and neurological problems, therefore the TLV should be considered as a LOAEL. There are some concerns that MIBK may potentiate the hexacarbon solvent (e.g. *n*-hexane)- or haloalkane solvent-induced neuropathy such as peripheral nerve degeneration and muscle weakness in the legs. Since MIBK occasionally exists as a component of solvent mixtures in industrial uses, this effect of MIBK needs to be considered in standard development.

The concerns of health effects that have occurred at the TLV-TWA level and the possible potentiation of adverse effects of other solvents suggest that the New York State's SGC (1-hour averaging) may not be the most appropriate criterion to derive air quality standards for the protection of health for the general public. The State of Michigan used a conversion factor of 100 to derive its ITSL of 2,050 $\mu\text{g}/\text{m}^3$. Converting this 8-hour average ITSL to a half-hour averaging equivalent limit yields a value of 4,100 $\mu\text{g}/\text{m}^3$, which is higher than MOE's odour-based POI of 1200 $\mu\text{g}/\text{m}^3$. Furthermore, the derivation of the ITSL does not take into account that adverse effects have been reported in workers exposed at the TLV-TWA.

Based on the same TLV-TWA of the ACGIH, the State of Massachusetts has derived its 24-hour average TEL (Threshold Effects Exposure Limits) of 55.7 $\mu\text{g}/\text{m}^3$. The uncertainty factors include: 4.2 to account for continuous exposure; 1.75 to account for differences in sensitivity between adults and children; 10 to account for high-risk groups and other sensitive sub-populations; 10 to account for incomplete data in the toxicity database used to review the potential toxicity of MIBK; and a factor of 5 for multimedia exposure. Since air is the main route of exposure, a multi-media factor (5) is not considered necessary. Considering that a factor of 10 is added for high risk groups, and another factor of 10 for the limited information available, an additional factor of 1.75 for differences in sensitivity between adults and children does not seem necessary.

The odour thresholds for MIBK have been reported to be between 0.1 and 7.8 ppm (400 and 32,000 $\mu\text{g}/\text{m}^3$) with a geometric mean of 3,600 $\mu\text{g}/\text{m}^3$. The present MOE's odour threshold-based POI of 1,200 $\mu\text{g}/\text{m}^3$, which is at the low end of the reported odour thresholds and is comparable to the health-based guidelines.

Based on limited ecological data, MIBK is not expected to be deleterious to terrestrial and aquatic organisms at the current POI and AAQC levels.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has

evaluated and agreed with the states of Massachusetts, Michigan and New York and accepts the scientific studies which support the development of the occupational exposure limit of 205,000 $\mu\text{g}/\text{m}^3$ from the ACGIH (TLV-TWA) and the NIOSH (REL). After reviewing additional toxicological information, the Ministry has considered that air quality standards for MIBK can be derived based on the rationale for this occupational exposure limit. The TLV-TWA of 205,000 $\mu\text{g}/\text{m}^3$ is divided by a factor of 1.5 to convert from an 8-hour work day exposure to a 24-hour equivalent averaging time (MOE, 1987). A total uncertainty factor of 100 is applied which includes a factor of 10 since the occupational exposure limit is based on an apparent LOAEL, rather than a no-observable adverse effect level (NOAEL), and a factor of 10 for protecting sensitive individuals. Applying these factors to the TLV-TWA could result in a 24-hour criterion of 1,366 $\mu\text{g}/\text{m}^3$ which is in close agreement with the current odour-based 24-hour AAQC. Deriving a 24-hour AAQC from TLV-TWA will result in a criterion higher than the current Ontario odour-based 24-hour AAQC. Therefore, replacing the odour-based POI and 24-hour AAQC of 1,200 $\mu\text{g}/\text{m}^3$ is not recommended.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, the odour property of this compound, and comments received from stakeholders, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for methylisobutyl ketone:

- a 24-hour average AAQC of 1,200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for MIBK, based on the odour nuisance, the adverse health effects and the potential interaction with other hydrocarbon solvents of this compound; and,
- a half-hour average POI of 1,200 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for MIBK, based on the odour nuisance of this compound. This odour based POI is also protective of health.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of

models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for methylisobutyl ketone can be sent to:

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State of Michigan, 1997. List of Screening Levels (ITSL, IRSI, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

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US EPA, 1997. Integrated Risk Information System Computerised Database. United States Environmental Protection Agency, Washington, DC.

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS# 108-10-1)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The Reference concentration (RfC) for inhalation exposure is under review. MIBK has not been evaluated for evidence of human carcinogenic potential. No ambient air exposure limits are defined.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

No air quality guideline currently exists.

8. *Key Risk Assessment Considerations:*

No information available.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

No information available.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for MIBK. No risk-based concentration limit has been established for MIBK.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be prioritized. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to determine the conditions under which these values should be interpreted and applied.

5. *Documentation Available:*

CAPCOA, 1993. Air Toxics "Hot Spots" Program - Revised 1992 Risk Assessment Guidelines. California Air Pollution Control Officers Association.

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 657-660.

6. *Peer-Review Process and Public Consultation:*

The draft Toxic Air Contaminant Identification list is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified under the Toxic Air Contaminants Identification list were taken from existing governmental exposure and health effects databases (eg., Hazardous Substances Database, Integrated Risk Information System, etc.) and additional widely recognised reference books.

The RfCs, reference exposure levels (REL's) and cancer potency values reported in both the draft Toxic Air Contaminant Identification list and the CAPCOA (1993) documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessments conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for MIBK. The State of California identifies that a reference concentration (RfC) for MIBK is currently under review by the US EPA (ARB, 1996).

MIBK is identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment" which is the State's next step in establishing a potential air quality guideline value (ARB, 1997).

9. *Key Risk Management Considerations:*

Not applicable

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). MIBK is not one of these substances.

11. *Other Relevant Factors:*

MIBK is identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) (24-hour averaging time) and the Allowable Ambient Limit (AAL) have both been set at $55.7 \mu\text{g}/\text{m}^3$. In cases where these levels are equivalent, the MDEP applies the averaging time of the TEL, i.e., 24 hours.

4. *Application:*

The TEL and AAL are to be employed in the permitting, compliance and enforcement of the State of Massachusetts air quality program. The primary goal of TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum to DEP/DPH Advisory Committee on Health Effects from the Office of Research and Standards, dated October 20, 1994. Revisions to Massachusetts Allowable Ambient Air Limits for Compounds with Inhalation Reference Concentrations.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1987. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US

EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. Status of Guideline:

Current. Guidelines may be updated periodically.

8. Key Risk Assessment Considerations:

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of MIBK, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH Threshold Limit Value - Time Weighted Average (TLV-TWA) occupational exposure limit for MIBK, has adopted the level of 204.70 mg/m³. For use in the MDEP air guidelines, this level was considered the Most Appropriate Occupational Limit (MAOL) and was adjusted by the following factors:

1. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week, to consider continuous exposure;
2. divided by 1.75 to account for differences in sensitivity between adults and children;
3. divided by 10 to account for high-risk groups and other sensitive sub-populations; and
4. divided by 10 to account for incomplete data in the toxicity database used to review the potential toxicity of MIBK.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, 735. The adjusted MAOL is numerically equivalent to 0.27850 mg/m³ (278.50 µg/m³). At this point, another set of uncertainty factors were applied to the adjusted MAOL:

1. divided by 1. The Threshold Effects Uncertainty Factor (TEUF) is an uncertainty factor which accounts for acute, chronic, developmental or reproductive effects that may not have been

-
- considered in the health risk assessment of the occupational exposure limit. The MDEP applied a score of 1 for MIBK; and
2. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 3,675. The TEL was, therefore, calculated as $55.70 \mu\text{g}/\text{m}^3$.

Non-Threshold Effects

The MDEP reported that there was inadequate evidence to classify MIBK's mutagenic potential. There was no positive evidence to classify MIBK's carcinogenic potential and a negative result/score for MIBK's structure activity relationship (SAR) analysis (MDEP, 1990). The Non-Threshold Effect Exposure Limit (NTEL) was developed from the adjusted MAOL ($278.50 \mu\text{g}/\text{m}^3$) using a Non-Threshold Effects Uncertainty Factor (NTEUF) of 1 which accounts for MIBK's scores in the carcinogenic, mutagenic and SAR analyses. No adjustment was made for multimedia considerations. The resulting NTEL for MIBK was calculated as $278.5 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the TEL for MIBK was adopted as the AAL. The MIBK AAL is $55.70 \mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in 1,000,000 (10^{-6}) or less.

The process of derivation of air guidelines does not include technological, economic or enforcement considerations.

10. Multimedia Considerations of Guidelines:

A factor of 0.2 was applied to the guideline to allow for contributions to exposure from media other than air.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* State of Michigan, Department of Environmental Quality (DEQ)

3. *Guideline Value(s):*

The 8-hour Initial Threshold Screening Level (ITSL) is 2,050 $\mu\text{g}/\text{m}^3$.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that toxic from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by the screening method approved by the Commission.

Screening levels for each air toxic are developed by the Air Quality Division of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan. 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan. 1992. R336.1230 Air Toxics from New and Modified Sources.

State of Michigan. 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan. 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

ACGIH, 1991. Documentation of the Threshold Limit Values and Biological Exposure Indices. Sixth Edition. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of this value. Specifically, ACGIH's process for development of TLVs, upon which the ITSL for MIBK is based, were employed.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The health assessment methodology by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for MIBK was determined from the Threshold Limit Value (TLV) established by the American Conference of Government Industrial Hygienists (ACGIH) and has an averaging time of 8 hours. The ITSL was determined by dividing the occupational exposure level (OEL) by 100. The 100 fold safety factor is derived as follows:

$$\begin{aligned} \text{ITSL} &= \text{OEL} \times A \times B \times C \\ &= \text{OEL} \times \frac{40 \text{ hours}}{168 \text{ hours}} \times \frac{30 \text{ years}}{70 \text{ years}} \times \frac{1}{10} \\ &= \frac{\text{OEL}}{100} \end{aligned}$$

where:

-
- A adjusts for the difference between a 40 hour work week and the total hours in a week; B adjusts for the difference between the number of years a person is assumed to work and the total estimated lifetime;
C adjusts for the possible higher susceptibility of certain individuals in the general population when compared to the healthy adult worker.

The ACGIH established a Threshold-Limit-Value-Time-Weighted-Average (TLV-TWA) of 50 ppm for MIBK (ACGIH, 1991). TLVs refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse health effects. A TLV-TWA is the time-weighted average concentration for a normal 8-hour workday and a 40-hour work week, to which nearly all workers may be repeatedly exposed without adverse effect (ACGIH, 1994).

With a conversion factor of $1 \text{ ppm} = 4.10 \text{ mg/m}^3$, 50 ppm is equivalent to 205 mg/m^3 or $205000 \text{ } \mu\text{g/m}^3$. This was divided by 100 to arrive at the ITSL of $2,050 \text{ } \mu\text{g/m}^3$.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

The ACGIH has stated that "These (TLVs) are intended for use in the practice of industrial hygiene as guidelines or recommendations in the control of potential health hazards and for no other use, e.g., in the evaluation or control of community air pollution nuisances, in estimating the toxic potential of continuous uninterrupted exposures..." (ACGIH, 1994). Therefore, the use of TLVs as a starting point in air quality guidelines is inconsistent with their intended use.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* New Jersey Department of Environmental Protection

3. *Guideline Value(s):*

The State of New Jersey has not identified any specific guideline for MIBK. A reference concentration (RfC) of 80 mg/m³ is recognized and applied for the purposes of conducting risk assessments under the Air Quality Permitting Program.

4. *Application:*

The New Jersey Department of Environmental Protection, Bureau of Air Quality Evaluation's Air Quality Permitting Program requires a proponent to complete a risk assessment in conjunction with applying for an air pollution control pre-construction permit. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which is listed on the Federal Hazardous Air Pollutants list posted under the Clean Air Act. The RfC for MIBK is identified for the purposes of completing such a risk assessment.

5. *Documentation Available:*

New Jersey Department of Environmental Protection. 1994. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

Key Reference(s):

US EPA. 1993. Health Effects Assessment Summary Table (HEAST). United States Environmental Protection Agency. Washington, DC.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The RfC referenced above should be used in the risk assessment to estimate the public health risks for inhalation of MIBK using the following equation:

$$\text{Hazard Quotient} = C / \text{RfC}$$

where C = maximum ambient air concentration in $\mu\text{g}/\text{m}^3$

RfC = Inhalation RfC = $80 \mu\text{g}/\text{m}^3$

This RfC is adopted from HEAST, 1993. HEAST is a summary of health effects levels derived by the US EPA. As the RfC for MIBK is under review by the US EPA, no RfC currently exists for MIBK. New Jersey has not adjusted the RfC in light of the on-going review by the US EPA (NJDEP, 1997a). The maximum annual average ambient air concentrations of pollutants (C) are derived from one of three approaches: an initial risk screening assessment, dispersion modelling, or air monitoring programs (NJDEP, 1997a). In the case of MIBK, air monitoring programs have little information on its annual average concentrations (NJDEP, 1997a).

Hazard indices which are less than or equal to one indicate a risk which is considered to be negligible. However, hazard indices which are greater than one represent risks which are of concern to the State, and will be evaluated and managed on a case-by-case basis.

9. *Key Risk Management Considerations:*

The RfC is not a guideline or standard for MIBK. However, the State does identify MIBK as a Toxic Air Contaminant.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources

3. *Guideline Value(s):*

Short-term Guideline Concentration (SGC) is 48,000 $\mu\text{g}/\text{m}^3$ (equivalent to 48 mg/m^3 for 1-hour average). Annual Guideline Concentration (AGC) is 480 $\mu\text{g}/\text{m}^3$ (0.48 mg/m^3).

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Daft. New York State Department of Environmental Conservation, Division of Air Resources.

Key Reference(s):

NIOSH. 1988. NIOSH Recommendations for Occupational Safety and Health Standards. U.S. Department of Health and Human Services. Public Health Service. National Institute of Occupational Safety and Health (NIOSH), Centres for Disease Control, Atlanta, Georgia. Morbidity and Mortality Weekly Report. Vol. 37. No. S-7. August 26, 1988.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. *Key Risk Assessment Considerations:*

MIBK is classified as a moderate toxicity air contaminant (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The SGC was derived from NIOSH Recommended Exposure Limit-Time Weighted Average (REL-TWA) (1988) of 50 ppm by dividing the NIOSH REL-TWA by 4.2. The AGC was derived by dividing the REL by 420.

The factor used above as the divisor to adjust the occupational limit is based on adjusting 8 hour/day, 5 days/week occupational exposure to 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2). To compensate for applying occupational guidelines to the general population in establishing an AGC, an additional factor of 10 is used for contaminants defined as low toxicity chemicals and a factor of 100 is used for contaminants defined as moderate toxicity chemicals.

9. *Key Risk Management Considerations:*

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guideline considers only human exposure to contaminants in the air.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*
None.

4. *Application:*
None.

5. *Documentation Available:*
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series, No. 23. World Health Organization, Regional Office of Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*
Not applicable.

7. *Status of Guideline:*
Not applicable.

8. *Key Risk Assessment Considerations:*
None.

9. *Key Risk Management Considerations:*
None.

10. *Multimedia Considerations of Guidelines:*
None.

11. *Other Relevant Factors:*
None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)
2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

MIBK is classified as a class 3 gaseous organic substance (O.3). This classification imposes an emission standard of 150,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 3.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992).

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardize the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorized into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance, or a class of substance, exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office, Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment, The Hague, The Netherlands.

6. *Peer-Review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 150 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 3.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

9. *Key Risk Management Considerations:*

These standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the Environmental Protection Act.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS# 108-10-1)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*
No information available.

4. *Application:*
No information available.

5. *Documentation Available:*
Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*
No Information available.

7. *Status of Guideline:*
No information available.

8. *Key Risk Assessment Considerations:*
No information available.

9. *Key Risk Management Considerations:*
No information available.

10. *Multimedia Considerations of Guidelines:*
No information available.

11. *Other Relevant Factors:*
No information available.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Methylisobutyl Ketone (MIBK) (CAS # 108-10-1)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

None established. MIBK has not been assessed or evaluated under the Priority Substance List (PSL) 1 and is not listed for evaluation under PSL2.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a PSL that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada PSL2 Secretariat October 1995. Report of the Ministers' Expert Advisory Panel on the second Priority Substances List Under the Canadian Environmental Protection Act (CEPA). October 1995.

6. *Peer-Review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

None.





12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RFc	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
MINERAL SPIRITS**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**



Executive Summary

The Ontario Ministry of the Environment (MOE) has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Mineral spirits, particularly Stoddard solvent, were identified as priority compounds for review based on their patterns of use in Ontario. A review of the scientific and technical information relevant to setting ambient air quality standard for mineral spirits has previously been provided to stakeholders for comment. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for mineral spirits.

Mineral spirits, also called petroleum distillates, are liquid mixtures of at least 200 different hydrocarbons, primarily consisting of C_7 - C_{12} alkanes (paraffins) and cycloalkanes (naphthenes), with 15-20 % aromatic hydrocarbon content, of which less than 0.1 % is benzene. Due to the complex variable composition of mineral spirits, these solvent mixtures are often recognized using the names of the most commonly used commercial mixtures, including Stoddard solvent, VM & P naphtha, Varsol and white spirits. All are obtained by distillation of crude oil. These solvents have similar compositions and properties and are widely used in dry-cleaning fluids, paint thinners, varnishes, photocopy toners, inks, adhesives, and as general purpose cleaners and degreasers.

The major source of mineral spirits in ambient air are dry-cleaning facilities, spills, and waste sites. There is no information regarding releases or ambient air concentrations of these solvents in Ontario, nor was any other information in the literature about the ambient air levels. Since these solvents are complex and variable mixtures, their concentrations cannot be measured accurately and specifically in air. Information on their atmospheric levels may be estimated using dispersion modelling through the presence of individual volatile chemical components. Using the modelling method the US Environmental Protection Agency (EPA) estimated that in the Chicago area the maximum exposure level to Stoddard solvent, due to potential industrial waste streams, is $103 \mu\text{g}/\text{m}^3$. Standardized methods of measurement (concentration and adsorption on a solid sorbent) have been developed for the workplace with a percentage recovery of all components of up to 90 %. The detection limit for mineral spirits ranges from 2,500 to 5,000 $\mu\text{g}/\text{m}^3$.

When mineral spirits are released in air from a point source, all chemical components are differentially evaporated and dispersed in the surrounding ambient air according to their individual physical and chemical properties. The initial concentration ratios of all components of the solvent mixture at the point of emission will not be expected to space away from the point source. This makes the positive identification of a particular hydrocarbon mixture in ambient air very difficult. Additionally, many components of these solvents are commonly released by other sources such as automobile exhaust and

oil, and can easily be confused with background levels. In the context of diffuse sources of emissions, such as waste sites, the task of identifying and quantifying hydrocarbon solvents over the background level is even more complex.

Mineral spirits are expected to induce primarily non-cancer effects. Mineral spirits cause adverse health effects such as eye, throat, respiratory tract, reproductive, and neurological problems. The major threat posed by these solvents is from long-term or chronic exposures. Data on cancer development related to Stoddard solvent is inconclusive, but concerns have been raised over the probable carcinogenicity and genotoxicity of other petroleum distillates like machining/cutting oils in the workplace following chronic exposure to much higher doses.

The current Ontario 24-hour average air quality criterion for mineral spirits is set at $10,000 \mu\text{g}/\text{m}^3$ on the basis of health. The half-hour Point of Impingement (POI) guideline is set at $30,000 \mu\text{g}/\text{m}^3$ on the basis of odour.

In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Only the State of Michigan has a recommended guideline (ITSL, Initial Threshold Screening Level) for the combined impact of all petroleum hydrocarbon solvent mixtures of $3,500 \mu\text{g}/\text{m}^3$ and is based on an 8-hour average. Some specific components of the mixture are designated with annual average guidelines which were derived from available NOAEL or LD_{50} . The lack of established guidelines for mineral spirits from the above mentioned agencies prompted the examination of guidelines from several other additional State agencies. Most of the guidelines of these agencies were derived from occupational exposure limits, although the values and averaging times are different.

For protection of human health, guidelines have been derived from occupational exposure levels. The odour detection threshold of mineral spirits (in the range of 2000 to $5250 \mu\text{g}/\text{m}^3$) indicate that odour may also be a concern with mineral spirits.

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and agreed with the State of Michigan and accepts the scientific studies which support the development of the occupational exposure limit of $350,000 \mu\text{g}/\text{m}^3$ from the National Institute for Occupational Safety & Health. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for mineral spirits based on the rationale for this occupational exposure limit. Applying an exposure time conversion factor and appropriate uncertainty factors to the

Threshold Limit Value -Time-weight Average of 350,000 $\mu\text{g}/\text{m}^3$ result in a 24-hour AAQC of 2,600 $\mu\text{g}/\text{m}^3$. In addition, the Ministry has also considered the odour effect of mineral spirits in deriving its air quality standards. The odour thresholds for Stoddard solvent and mineral spirits range from 500 to 5250 $\mu\text{g}/\text{m}^3$. In the absence of a geometric mean for odour thresholds, the arithmetic mean of values at the two ends of the range is used to derive an odour-based POI.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and the odour nuisance of mineral spirits, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for mineral spirits:

- a 24-hour average AAQC of 2,600 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for mineral spirits based on the adverse health effects of this compound; and,
- a half-hour average POI standard of 3,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for mineral spirits based on the odour nuisance of this compound.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Mineral spirits, including Stoddard solvent, were identified as a priority for review based on their pattern of use in Ontario. A review of scientific and technical information relevant to setting an ambient air quality standard for mineral spirits had been provided in a previous document and was distributed to stakeholders for their comments. This document provides the rationale for recommending an AAQC and a POI standard for mineral spirits.

2.0 General Information

2.1 Physical/chemical Properties

Mineral spirits are colourless petroleum distillate mixtures of C_7 - C_{12} hydrocarbons (generally >65% C_{10} and higher), with boiling points ranging from 130-220°C and flash points ranging from 21-60°C. These solvent mixtures have been identified by various names and synonyms, including Stoddard solvent, dry cleaning safety solvent, petroleum solvent, varnoline, spotting naphtha, white spirits, petroleum distillates, petroleum spirits, ligroine, VM & P naphtha, benzine and trade named products such as Varsol, Solvesso and Petrosol. The Chemical Abstracts Service (CAS) identification numbers for some of these solvents are as follows:

Naphtha	8030-30-6
Ligroine	8032-32-4
Stoddard solvent	8052-41-3
Heavy hydrotreated petroleum naphtha	64742-48-9
Medium aliphatic solvent petroleum naphtha	64742-88-7
Light aliphatic solvent petroleum naphtha	64742-89-8

All of these are liquid mixtures, which are primarily composed of 30-50% linear and branched alkanes, 30-40% cycloalkanes and 5-20% aromatic hydrocarbons (<0.1% benzene; mainly alkylbenzenes particularly trimethylbenzene), formed in the standard production of petroleum. More specifically, all of the mineral spirit formulations are comprised of three classes of compounds: the alkanes (*n*-nonane, -decane, methylnonanes, 2,6-dimethyloctane, *n*-undecane, dodecanes, tridecanes), the cycloalkanes (monocycloparaffins, dicycloparaffins, tricycloparaffins, acenaphthenes) and aromatic compounds. The latter include alkylbenzenes (dimethylbenzenes, *n*-propylbenzene, ethyltoluenes, 1,2,4-trimethylbenzene, toluene, xylenes), other benzenes, indans/tetralins, indenenes, naphthalenes, acenaphthalenes, and tricyclic aromatics. Alkylbenzenes account for most of the contribution of the aromatics to the total chemical composition of these solvents while the rest of the aromatics account for no more than 4.6% of the total; each chemical species rarely contributing more than 1% individually. Very few of the aromatics are individually classifiable as human carcinogens except for benzene.

Mineral spirits have a sweet odour similar to kerosene. The odour detection threshold is reported to range from 2,000 to 5,250 $\mu\text{g}/\text{m}^3$ (ATSDR, 1995; Ruth, 1986), and is expected to vary because of the variable chemical composition of these mixtures. The odour irritation concentration of Stoddard solvent is 2,100,000 $\mu\text{g}/\text{m}^3$ (Ruth, 1986). Odour thresholds, which have been reported in some human volunteers, for Stoddard solvent range between 500 to 5,000 $\mu\text{g}/\text{m}^3$ (Carpenter *et al.*, 1975 as cited in NIOSH, 1977a). These solvents are considered hazardous materials for which transportation and

management is regulated. Disposal of these compounds is recommended through controlled incineration. Disposal to domestic sewage drains is prohibited.

2.2 Uses of Mineral Spirits

Mineral spirits are industrial multipurpose organic solvents widely used in dry-cleaning products, inks, paints and thinning agents for paints, coatings, waxes, varnishes, adhesives, photocopy toners, machine shop and automotive repair applications, and as cleaners and degreasers. The major industries most commonly associated with these solvents are electroplating, metal degreasing, paint stripping, semiconductors and dry-cleaning. Although one type of mineral spirit, Stoddard solvent, was introduced in the 1920's specifically for use in dry-cleaning, most dry-cleaners today use chlorinated hydrocarbon solvents such as perchloroethylene rather than mineral spirits.

2.3 Sources and Levels

Mineral spirits are detected in the air through their individual components. There are standardized methods for measuring their concentration in air. These methods are approved by the National Institute for Occupational Health and Safety, method 1550 (NIOSH, 1984), and by the Occupational Safety and Health Administration (OSHA), method 48. For these methods, the analytical precision is good but not all of the components present in the air are easily recovered (i.e., less than 90% are recovered) and the detection limit of the equipment is poor (i.e., requires $5,000 \mu\text{g}/\text{m}^3$ as a total concentration). Other methods need to be developed for a better recovery of all the components. At present, knowledge on the exact hydrocarbon components and their ratios in various hydrocarbon mixtures in air (e.g. Stoddard solvent versus paint thinners) is scarce.

Mineral spirits are mainly released to the atmosphere from industrial facilities, waste sites, and as a result of large spills into soil and water. Volatilization along with subsequent rapid photooxidation in the atmosphere is expected to be an important fate of mineral spirit releases. An experiment designed to determine the potential hazard to operators of landfill sites by comparing the volatilization of Stoddard solvent on a simulated waste site and a nearby lagoon, reported a rate of evaporation six times greater from the solid waste site. Mineral spirits are not listed as candidate pollutants on Environment Canada's National Pollutant Release Inventory for environmental release reporting by industry (NPRI, 1997). In the US, based on information in the 1990 Toxics Release Inventory, reporting releases of Stoddard solvent was not mandatory. However, the total volume of production was estimated to have dropped by 51%, from 74.9 million pounds in 1986 to 38.3 million pounds in 1990. The average concentration of Stoddard solvent emitted from one dry-cleaning plant was determined to be in the order of $12,033,000 \mu\text{g}/\text{m}^3$ measured as propane (ATSDR, 1995).

The MOE has not measured, or estimated, ambient air levels of mineral spirits in Ontario (MOEE, 1997). Given the difficulty in measuring mineral spirits *per se* in ambient air, no data on these levels could be located in the literature. Some estimation of population exposure was established by the US EPA, in the Chicago area, using air dispersion models for five combustion scenarios at the emission source. The highest concentration of Stoddard solvent to which people would be exposed to in ambient air, expressed as a total concentration, was predicted to be $103 \mu\text{g}/\text{m}^3$ (ATSDR, 1995). In comparison, indoor air levels of Stoddard solvent in paint booths was found to be in the range of 412,000 to 707,000 $\mu\text{g}/\text{m}^3$ (Bradley and Bodsworth 1983). The occupational exposure would then appear to be thousands of times more than values predicted by dispersion models for ambient air. However, with a detection limit of $5,000 \mu\text{g}/\text{m}^3$, the current standard methods of measurement for mineral spirits used for indoor air levels would not appear to be sensitive enough for detecting the anticipated lower ambient air levels even if "mineral spirits" *per se* could be measured with certainty.

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 74 facilities with emissions of mineral spirits covered by a Certificate was identified. These approvals were for emissions from manufacturers of plastic products, transportation equipment, forest product and metal and mining industries and chemical plants. The median Ground Level Concentration estimated by Regulation 346 dispersion modelling for all 74 sources was approximately $59.35 \mu\text{g}/\text{m}^3$. The maximum and minimum were 5854 and $0.002 \mu\text{g}/\text{m}^3$, respectively.

2.4 Environmental Fate

The environmental fate of mineral spirits will depend on the physico-chemical and biological properties of the constituents. The lower molecular weight alkanes and aromatics tend to volatilize and undergo photodegradation in the atmosphere. Higher molecular weight compounds tend to adsorb to organic matter in soil or water. Biodegradation of C_7 to C_{12} hydrocarbons is expected to be significant under conditions favourable for microbial oxidation. Mineral spirits have a moderate potential for bioaccumulation based on octanol-water partitioning coefficients of 3.5 to 6.4, however, the likelihood of bioconcentration in the environment is reduced by degradation and reduced bioavailability resulting from sorption to organic matter (WHO, 1996).

3.0 Toxicology of Mineral Spirits

Contact with mineral spirits generally occurs as a result of inhalation or through the skin. Exposure to mineral spirits can cause skin, eye and throat irritation, and dermatitis. No studies were found on the effects of solvents following ingestion. The inhalation and dermal routes are the most predominant routes of exposure, but it is still unclear which one is the most significant. Once the solvent enters the

body, it quickly enters the bloodstream. At present there is no reliable information regarding doses of mineral spirits that could lead to death in humans (ATSDR, 1995).

3.1 Acute Toxicity

Inhalation of mineral spirits causes dizziness and headaches. Studies have been performed on human volunteers to investigate short-term or acute toxicological effects and biochemical changes following inhalation of white spirits (Shellsoll TS: 99% paraffins; Exsol D 40: 52% paraffins and 48% naphthenes; Varnolene: 57% paraffins, 25% naphthenes and 18% aromatics) for 6 or 48 hours. Inhalation of any of the three white spirits at a concentration of approximately 102 ppm (605 - 610 mg/m³) or to Exsol D 40 at 0, 51, 102 and 205 ppm (0, 304, 611 and 1228 mg/m³) did not induce the symptoms reported at higher concentrations such as dryness of the mucous membranes, loss of appetite, nausea, vomiting, diarrhoea, and fatigue during and after exposure. No symptoms were found which are usually associated with organic solvent poisoning such as headache, dizziness, feeling of inebriation, visual disturbances, tremour, muscle weakness, coordination impairment, or paraesthesia of the skin. The only biochemical changes observed were significant decreases in serum α -amylase 6 hours after exposure and in S-urate 48 hours following exposure to white spirit with high naphthalene content at 200 ppm (1228 mg/m³) (Pedersen and Cohr, 1984). This concentration was approximately equivalent to the TLV level of 100 ppm for light or moderate work, as explained by the authors.

A NOAEL of 140,000 $\mu\text{g}/\text{m}^3$ for a 15-min average and of 600,000 $\mu\text{g}/\text{m}^3$ for a 30-min average exposure were found for ocular effects, probably due to the direct contact of the concentrated vapours with the eyes (ATSDR, 1995).

3.2 Subchronic/chronic Toxicity

Long-term exposure studies on human volunteers suggested that the most sensitive indicator of chronic effects relates to neurological problems. In painters for example, a relationship was found between long-term hydrocarbon solvent exposure and a higher frequency of early disability pension due to neuropsychological disorders (Soren *et al.*, 1996).

Inhalation studies on animals showed that the hydrocarbons, which compose mineral spirits, may be stored in body fats and can enter the brain days after exposure to induce delayed effects. Stoddard solvent has been shown to cause seizures in rats, cats, and dogs, and bronchitis in guinea pigs. It has also been shown to cause kidney damage only in male rats. This is thought to be due to a specific protein, $\alpha_2\mu$ -globulin, which is synthesized in large amounts by male rats as a urinary pheromone carrier and is reabsorbed in the proximal tubules. Stoddard solvent may bind to this protein and accumulate in lysosomes in the proximal tubules where it causes nephropathy (ATSDR, 1995). No studies

established a possible link between exposure to Stoddard solvent and immunological or lymphoreticular effects (ATSDR, 1995).

3.3 Developmental/Reproductive Toxicity

Stoddard solvent was not found to cause maternal toxicity, structural teratogenesis, or decreased foetal weight when administered during organogenesis in the rat. No studies have established a possible link between exposure to Stoddard solvent and birth defects, reproductive effects, and/or infertility (ATSDR, 1995).

3.4 Genotoxicity

The lack of mutagenic activity of white spirits was reported by Gochet *et al.* (1984) with different strains of *Salmonella typhimurium* as well as in *in vivo* animal studies. However, the available data is much too limited to allow definitive conclusions regarding the genotoxicity of mineral spirits in humans. There is some concern regarding the genotoxicity of some components of mineral spirits. As mentioned above, *n*-decane will increase the frequency of mutations in V79 Chinese hamster cells in the presence of methylazoxymethanol, although it does not cause mutagenesis on its own. This suggests that *n*-decane may be a cancer promoter. It is not certain whether some of the carcinogenic and genotoxic effects observed with some of the individual components of these solvents would also occur with the complete mixture.

3.5 Carcinogenicity

Few studies were conducted on the carcinogenic effects of mineral spirits in humans and animals. The International Agency for Research on Cancer (IARC) classifies "petroleum distillates" as probable human carcinogens. However, these mixtures have not been classified as carcinogenic by the American Department of Health and Human Services (DHHS), the US EPA, or any other national or international agencies in any exposure situation (ATSDR, 1995). A limited case-referent study using cases of Hodgkin's and non-Hodgkin's lymphoma among Swedish workers exposed to white spirits implied a slight increase in crude odds ratios (ORs), but was limited by an insufficient number of cases (Persson *et al.*, 1993). Some human data were obtained from a case-control study of 32-100 individuals who had cancer and were questioned on their exposure to unknown levels of petroleum products (Siemiatycki *et al.*, 1987). Statistically significant ORs were found for mineral spirits and prostate cancer. Non-significant but positive ORs were reported for Hodgkin's lymphoma and squamous cell carcinoma of the lung.

It has been estimated that 75% of dry cleaners world-wide now use tetrachloroethylene; the remaining 25% use petroleum-based solvents. The carcinogenic risk for people working in dry cleaning facilities

and exposed to Stoddard solvent, trichloroethylene, and carbon tetrachloride was evaluated (McGregor *et al.*, 1995). The relationship between employment in dry cleaning and cancer incidence was assessed in studies of proportionate mortality in case-referent studies and in cohort studies. Risks were evaluated for urinary, bladder and oesophageal cancer. It was found that dry cleaning entails exposures that are possibly carcinogenic to humans. However, none of these studies provide conclusive results on the carcinogenic potential of mineral spirits for humans exposed at ambient air levels, such as at hazardous waste sites.

There was only one chronic dermal (skin-painting) study in mice that was suggestive of possible carcinogenic effects of mineral spirits, although the results were considered ambiguous as the test substance was a rust-preventative compound containing not only Stoddard solvent (90%) but also calcium petroleum sulphonate (7%) and ethylene glycol monobutyl ether (3%). Several other studies have shown that carcinogenesis cannot be attributed to any particular component of mineral spirits, however, *n*-alkanes may be one of the promoters of carcinogenicity or co-carcinogenic elements. An *in vitro* study on V79 Chinese hamster cells showed that *n*-decane, a component of mineral spirits, may be a tumour promoter since the frequency of mutations caused by methylazoxymethanol, a complete carcinogen in several species, increased in the presence of *n*-decane (ATSDR, 1995). In contrast, some other components of mineral spirits, such as the alkylbenzenes, are believed not to be carcinogenic (ATSDR, 1995).

3.6 Environmental Effects

There have been very few studies on the toxicity of mineral spirits to wildlife. The application of Stoddard solvent (1,123 L/ha) to the excised root tips of various species of pine seedlings resulted in an increase in oxygen uptake ranging from 19% to 39% (Voigt, 1953). Aquatic organisms exposed to mineral spirits have demonstrated LC₅₀ values ranging from 0.5 to 5 mg/L (WHO, 1996).

4.0 Existing Ambient Air Quality Criteria

4.1 Overview

MOE has a current AAQC and a POI guideline for mineral spirits (MOEE, 1994), which are intended to limit the release of a variety of petroleum distillates to ambient air. The current 24-hour average AAQC is set at 10,000 µg/m³ on the basis of health, and the half-hour POI guideline was is at 30,000 µg/m³ on the basis of odour.

In revising the air quality standards for Ontario, the MOE is considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for

air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey and Michigan, The Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency-specific summaries of guidelines for mineral spirits are presented in Section 7. A brief summary of available criteria is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the MOE typically uses a factor of 15 to convert from guidelines based on annual average concentrations to half-hour point-of-impingement limits, and a factor of 3 to convert from guidelines based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality guidelines based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of all the agencies reviewed, only Michigan refers to specific petroleum hydrocarbon solvent mixtures. Their 8-hour guideline (ITSL) of $3500 \mu\text{g}/\text{m}^3$ is for the combined ambient impact of all petroleum hydrocarbons other than mineral oils. In addition, Michigan has set different annual-average limits (e.g. $2 - 24 \mu\text{g}/\text{m}^3$) for some specific hydrocarbon solvent mixtures for which applicable NOAEL or LD_{50} were available to derive specific effect-based criteria. These values were applied to hydrotreated middle distillate, hydro-desulphurized middle distillate, sweetened middle distillate, hydrotreated heavy naphthenic distillate, and hydrotreated light distillate. The State of New York plans to set a guideline for Stoddard solvent in the near future which will be based on the occupational limit of $350,000 \mu\text{g}/\text{m}^3$ of the US National Institute for Occupational Safety and Health (NIOSH), using a method similar to that of Michigan. The State of New York also intends to establish an equivalent concentration to set a guideline for mineral spirits which refers implicitly to the total concentration of all hydrocarbon constituents of the mixture. The Netherlands refers to emission levels of organic hydrocarbon compounds which may include solvent mixtures.

Considering that only the state of Michigan has a guideline for hydrocarbon solvent mixtures among the listed agencies, guidelines in nine other State agencies (Connecticut, Florida-Pinellas, Florida-Ft. Lauderdale, Nevada, North Dakota, Oklahoma, Texas, Vermont and Virginia) were also reviewed (ATSDR, 1995; US EPA 1993). The guidelines from these states are based on similar occupational exposure limits but there are considerable variations among their air quality criteria. The recommended 8-hour average criteria vary between $3,500 \mu\text{g}/\text{m}^3$ and $7,000 \mu\text{g}/\text{m}^3$, the 24-hour average limits vary between $1,260$ and $8,800 \mu\text{g}/\text{m}^3$, and the annual average guidelines vary between 350 and $12,500 \mu\text{g}/\text{m}^3$. The scientific rationales for these guidelines are not available for evaluation.

Table 1. Summary of Existing Air Quality Guidelines¹ for Mineral Spirits

Agency	Guideline Value ²	Basis of Guideline	Date ³	Comments
Michigan	3,500 µg/m³ ITSL (8-hour average), total refined petroleum hydrocarbons (not including mineral oils); in addition, there are longer-term guidelines for specific solvent types: • hydrotreated middle distillate, hydro-desulphurized middle distillate, sweetened middle distillate: 2 µg/m³ ITSL (annual average) • hydrotreated heavy naphthenic distillate: 16 µg/m³ ITSL (annual average) • hydrotreated light distillate: 24 µg/m³ ITSL (annual average)	Occupational levels 1% of NIOSH REL NOAEL from unpublished API 4-wk rat inhalation study, 24 mg/m³ Surrogate acute oral LD₅₀ from 14-day rat gavage study, greater than 5 g/kg body weight NOAEL for deodorized kerosine from rat subchronic inhalation study, 98 mg/m³	1992	Initial threshold screening level (ITSL) of 3,500 µg/m³ for all hydrocarbon materials excluding mineral oils. NIOSH REL 350,000 µg/m³ Based on study on hydrodesulphurized middle distillate, others have similar composition Composition similar to deodorized kerosine, similar toxicity expected.
The Netherlands	none	emission standard of 100,000 µg/m ³ HC for flows of 2.0 kg per hour or more	1987	hydrocarbons (HC) in general
Canada (CEPA)	none		1997	Not in PSL-1 or PSL-2
Ontario	AAQC for mineral spirits 10,000 µg/m³ (24-hour average) 30,000 µg/m³ (half-hour POI)	Health Odour	1994	AAQC (Ambient Air Quality Criteria) Point Of Impingement guideline.

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- As different jurisdictions use different units to express concentration, an air concentration conversion factor of 1ppm = 5682 µg/m³ has been used whenever a conversion to µg/m³ was necessary to maintain a consistent unit of measure within this document (ATSDR, 1995).
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

In addition to agency guidelines, occupational exposure limits were also examined. Occupational safety and health agencies recommend workplace exposure limits by considering human health effects regarding the central nervous system (dizziness, headaches), the eyes, skin, throat, and odour irritations caused by mineral spirits. The OSHA set the maximum allowable concentration of refined petroleum solvents at $2,900,000 \mu\text{g}/\text{m}^3$ for its PEL-TWA (Permissible Exposure Level during an 8-hour workday and 40-hour work week). The ACGIH (American Conference of Government Industrial Hygienists) set a TLV-TWA at $525,000 \mu\text{g}/\text{m}^3$. The NIOSH set a recommended exposure level (REL-TWA time weighted average) at $350,000 \mu\text{g}/\text{m}^3$ for an 8-hour average for refined petroleum solvents including mineral spirits, Stoddard solvent, petroleum ether, rubber solvent, Varnish Makers' and Painters' naphtha and kerosene (NIOSH, 1977a).

4.2 Evaluation of Existing Criteria

Existing air quality criteria from various agencies (Table 1) appears to focus on the health concerns of mineral spirits on the central nervous system following inhalation exposure. Despite some concerns regarding the potential carcinogenic effects of Stoddard solvent in the workplace, none of the agencies reviewed assessed mineral spirits on the basis of carcinogenicity. The evidence of carcinogenicity of Stoddard solvent in the human and animal database is currently ambiguous and any observed carcinogenic effect may be due to the presence of small amounts of aromatic carcinogenic components in the solvent mixture, e.g. benzene which is specifically regulated in Ontario.

4.2.1 Discussion Based on the Adverse Effects of Mineral Spirits

Most agencies do not have guidelines for the specific types of mineral spirits due to the unresolved issue of their compositional variability and the complexity of their mixtures in ambient air. Only a Michigan guideline refers specifically to hydrocarbon solvent mixtures for permitting purposes and does not contain any actual measurements. Michigan's 8-hour average guideline of $3500 \mu\text{g}/\text{m}^3$ is set for a combined ambient impact for all petroleum hydrocarbons with hydrocarbon profiles similar to mineral spirits, i.e. refined petroleum hydrocarbon mixtures excluding aromatic hydrocarbon solvent mixtures and mineral oil-based solvent mixtures (Butterfield, 1993). The guideline was derived from an occupational exposure limit, 1% of the NIOSH's REL of $350,000 \mu\text{g}/\text{m}^3$, determined from human epidemiological, volunteers, and animal toxicological data. In addition to this, Michigan has different 24-hour or annual average guidelines for specific mineral spirits for which NOAELs or LD₅₀s were available (see Table 1). The ambient air quality guidelines from other US states did not provide sufficient information to examine the scientific basis for their criteria.

Most of the exposure to mineral spirits in ambient air occurs through inhalation. Unfortunately, due to the complex nature of mineral spirits and the lack of adequate detection methods for determining the ambient concentrations of these mixtures, the majority of toxicological studies have focussed on indoor

inhalation exposures of a completely vaporized mixture. Meanwhile human exposure scenarios in ambient air are likely to result in greater exposure to the more volatile fractions (e.g. aromatics) than the less volatile fractions. Indoor inhalation studies may overemphasise the effects of the less volatile aliphatic fractions, which are associated with acute effects e.g. irritation and narcosis. However, in the absence of other data, it may be considered reasonable to extrapolate human risks from the indoor inhalation studies to ambient air situations. This extrapolation would only be fully valid assuming that all components of mineral spirits could be maintained together as the predominant mixture in ambient air, which is typically not the case.

All studies conducted on mineral spirits have been based on indoor exposure as a whole (integrative approach), where the mixture maintains its chemical integrity. Previous studies have not considered toxic components individually (dissective approach) (Mauderly, 1993). The integrative approach is favoured by the US EPA and would probably be more appropriate for ambient air. However, this approach is better suited for simple mixtures rather than for complex mixtures (Seed *et al.*, 1995). It necessitates the calculation of a hazard index, which is the summation of the hazard quotient of each compound in the mixture being equal to the current dose divided by the maximum acceptable dose for that compound.

Adverse effects on the central nervous system-mediated motor coordination are common following acute exposure to mineral spirits. Cerebral atrophy, discoordination, dementia, headaches, memory deficits, and fatigue were reported in humans suffering from chronic exposure to solvents including white spirits. This implies that the central nervous system (CNS) effects may become more severe with prolonged exposure time. Mineral spirits may also compound the effects of other chemicals that cause central nervous system depression, such as alcohol, barbiturates, and medical anaesthetics (ATSDR, 1995). Few inhalation studies have been performed in animals to describe the effects of prolonged exposure to mineral spirits.

Mineral spirits are commonly used in Ontario. Residents in the vicinity of facilities producing or using these solvents may be at risk as a result of chronic air exposure. These solvents also have multimedia impacts. They contribute to the environmental impact of volatile organic compounds as ozone precursors. Alkylbenzenes, and the aromatics in general, are persistent in water and soil and have the potential to bioaccumulate in biota.

4.2.2 Discussion on Methods for Criteria Development

The evaluation of mineral spirits must take into consideration their significant toxicity, the difficulty in identifying their individual components in mixtures, the difficulty in monitoring specific individual mixture components, and the limited availability of documented guidelines available from other agencies and jurisdictions. Some methods for setting a guideline for a hydrocarbon mixture are discussed below.

Regulations have tended to focus on single air contaminants and not on mixtures which reflects the difficulty of accurately estimating personal exposures to multiple pollutants and assessing multiple health outcomes. To compound the difficulty of assessing the toxic effects of complex mixtures as a whole in ambient air, the complexity and components may vary as human activities influence the sources, as meteorology continuously alters the distribution and dilution of the pollutants, as components undergo chemical transformation (Samet and Speizer, 1993), and as background levels significantly interfere with the main chemicals. Even if the exact chemical contents of a particular petroleum hydrocarbon solvent were known at the point of emission, once it enters ambient air it would not be realistic to look for the mixture as its initial chemical signature.

Understanding the health effects of complex mixtures, in ambient air would require much more multi-disciplinary research. Even in indoor environments ATSDR, in conjunction with the US Department of Human and Health Services through the NTP (National Toxicology Program), have recognized that further data are needed to reduce or eliminate the uncertainties inherent to the current database on the human health assessment of Stoddard solvent (ATSDR, 1995). For example, many chronic studies on neurotoxicity in humans related to mixed solvent exposures do not measure the concentration levels of the solvents.

None of the agencies reviewed considered the risk of individual components of mineral spirits. At low doses the toxic effects of mixtures may be evaluated with the dose-additive approach. This assumes that all components dispersed in the air will induce the same toxic effect in the same organ system, through the same mechanism of action, as if they were alone. In a regulatory context only the main toxic compounds are considered therefore eliminating those at levels well below their respective thresholds. In the case of mineral spirits, the major components (alkanes and cycloalkanes) cause the mixture's primary neurological effects via a common mechanism of action, nonpolar narcosis, with potency proportionate to molecular weight. A narcosis-carbon chain length relationship has been observed and discussed for short-chain aliphatic alkanes of C₅ to C₈ (NIOSH, 1977b). It would therefore appear reasonable to evaluate the potential effects of a mineral spirit hydrocarbon mixture as an aggregate based on total mg hydrocarbon /m³. Another approach, referred to as the "reciprocal calculation procedure" (ECETOC, 1997), is a way to estimate occupational exposure levels (OELs) for various components of a hydrocarbon mixture according to their fraction (relative proportions in the mixture), i.e.:

$$\frac{1}{OEL_{HC\text{ mixture}}} = \frac{f_a}{OEL_a} + \frac{f_b}{OEL_b} + \dots + \frac{f_n}{OEL_n}$$

This appears to be a reasonable approach provided that OELs are available for the majority of hydrocarbons in the mixture and provided that their relative proportions in the mixture are known and

anticipated to remain reasonably stable from batch to batch. The Health & Safety Executive of the United Kingdom employed the reciprocal calculation procedure to derive a solvent mixture OEL of 553 mg/m³ for white spirit. This was based on a hydrocarbon composition of 52% alkanes $\geq$ C₇, 27% cycloalkanes $\geq$ C₇, 10% aromatics, 1% C₈ aromatics (xylenes) and 10% trimethylbenzenes (HSE, 1998). It would be possible to derive an environmental criterion for mineral spirits from this aggregate OEL, if this particular "white spirits" composition is acceptable as a surrogate for mineral spirits in general.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including mineral spirits, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of inhalation toxicological information examined by the Ministry; the rationales of the agency guidelines which the Ministry has considered appropriate for the development of air quality standards, specifically, the rationale supporting the occupational exposure limit of NIOSH from which the air quality guidelines of the State of Michigan based; as well as technical and economic impacts that may be anticipated as a consequence of the revision of the air quality standards.

During the consultation period the Ministry received four submissions from various stakeholders regarding the draft document for mineral spirits. Comments from the automotive manufacturing stakeholders suggested that the odour-based POI for mineral spirits be maintained at its current level until more relevant information is available for an in-depth revision, for example, the report on risk assessment of total petroleum hydrocarbons produced by the TPH Criteria Working group in the U.S.A. One automotive equipment and parts manufacturing stakeholder explained that it would be technically difficult to monitor the emissions of subfractions of mineral spirits based on the guidelines developed by the State of Michigan and therefore recommended the current POI be maintained. A rubber industry stakeholder expressed concerns over the basis of the TLV-TWA for air quality standards derivation. The petroleum products stakeholders indicated that a full risk management process would be required if the Ministry intended to introduce a substantial decrease in the air quality standards for mineral spirits.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for

stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for mineral spirits. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder inputs regarding the economic impacts and technical feasibility of achieving the standard. In some cases the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for Mineral spirits

The current 24-hour average AAQC for mineral spirits is set at $10,000 \mu\text{g}/\text{m}^3$ on the basis of health, and the half-hour POI guideline is currently set at $30,000 \mu\text{g}/\text{m}^3$ on the basis of the odour effects of this compound. In the MOE documentation, mineral spirits is represented by the CAS Registry number for Stoddard solvent (CAS # 8052-41-3).

The odour detection thresholds for Stoddard solvent have been reported to be in the range of 500 to $5,000 \mu\text{g}/\text{m}^3$, whereas for mineral spirits they are in the range of 2000 to $5250 \mu\text{g}/\text{m}^3$. These values are at least one order of magnitude lower than the current POI. The aesthetic effect (odour) of mineral spirits is a critical effect to be considered in the development of air quality standards for Ontario.

The toxic effects of mineral spirits appear to be predominated by the adverse neurological effects of their major components such as alkanes and cycloalkanes. Brief exposure to levels above $140,000 \mu\text{g}/\text{m}^3$ may induce irritation of the eyes. Exposure to higher concentrations may result in adverse effects ranging from ocular and nasal irritations to headache, dizziness, nausea, narcosis and discoordination. Loss of appetite, aplastic anaemia, liver and kidney damage have also been reported. In light of the adverse neurological effects of mineral spirits, the NIOSH has established 8-hour TWA value ($350,000 \mu\text{g}/\text{m}^3$) for refined petroleum solvents, including mineral spirits and Stoddard solvent, as well as for aliphatic alkanes ($\text{C}_3 - \text{C}_8$). Most jurisdictions have used occupational exposure levels to derive their guidelines for mineral spirits or related hydrocarbon mixtures.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed, the Ministry has evaluated and agreed with the State of Michigan and accepted the scientific studies which support the development of the occupational exposure limit of $350,000 \mu\text{g}/\text{m}^3$ from the NIOSH. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for mineral spirits based on the rationale for this occupational exposure limit. The TLV-TWA of $350,000 \mu\text{g}/\text{m}^3$ is divided by a factor of 1.5 to convert from an 8-hour work day exposure to a 24-hour equivalent averaging time (MOE, 1987). A total uncertainty factor of 90 is applied which includes 3 for the insufficient database for mineral spirits, 3 for the exposure limit which is based on a mixture of hydrocarbons including alkanes, in which the neuropathological *n*-hexane may be a component and a factor 10 for protecting the sensitive individuals. Applying these factors to the TLV-TWA results in a 24-hour AAQC of $2,600 \mu\text{g}/\text{m}^3$.

The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). In addition, the Ministry has also considered the odour effect of mineral spirits in deriving its air quality standards. The odour thresholds for Stoddard solvent and mineral spirits range from 500 to $5250 \mu\text{g}/\text{m}^3$. In the absence of a geometric mean for odour thresholds, the arithmetic mean of values at the two ends of the range is used to derive an odour-based POI.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and the odour nuisance of mineral spirits, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for mineral spirits:

- a 24-hour average AAQC of $2,600 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for mineral spirits based on the adverse health effects of this compound; and,
- a half-hour average POI standard of $3,000 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for mineral spirits based on the odour nuisance of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above

recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard in the near term, a submission from a company subject to the standard should include the following information:

- The operations or processes which give rise to emissions of the substance(s) under review;
- The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
- Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
- 4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
- 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility, and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg.

346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility, and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for mineral spirits this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent a submission addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, "*Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998*" may assist you in completing the air emissions compliance assessment with the proposed air standard;

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- MOE Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects" Economic Services Branch- April 1994, and;
 - "Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for mineral spirits can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Mineral spirits

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

There is no reference in the US Environmental Protection Agency (EPA) database IRIS (Integrated Risk Information System).

4. *Application:*

IRIS contains health risk assessment information on over 300 chemicals. IRIS supports regulatory actions on a given compound but does not constitute a standard or guideline by itself. Since Stoddard solvent does not appear on the list of IRIS compounds, there is no application for Stoddard solvent. However, the DOT (Department of Transportation, Code of Federal Regulations, puts Stoddard solvent among the list of hazardous materials of 1989.

5. *Documentation Available:*

US EPA, 1995. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, D.C.

6. *Peer Review Process and Public Consultation:*

In its assessment, US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed. The National Toxicology Program on which IRIS bases its information, in conjunction with ATSDR (1995) has identified the need for further information on Stoddard solvent.

7. *Status of Guideline:*

No guideline. However, mineral spirits contain hydrocarbons (volatile organic compounds) which are regulated under the Clean Air Act guidelines for the reduction of VOC emissions from solvents (Clean Air Act 1990).

8. *Key Risk Assessment Considerations:*

No risk assessment considerations available.

9. *Key Risk Management Considerations:*

None, since no guidelines for ambient air exist.

10. *Multimedia Considerations of Guidelines:*

None are reported.

11. *Other Relevant Factors:*

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Mineral spirits

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

There is no reference in CAPCOA (1996).

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results have to be prioritized. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and resubmission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. Therefore, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

Key reference(s):

CAPCOA, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines. Report of the Risk Assessment Advisory Committee, 179 pp. + Appendices.

6. *Peer Review Process and Public Consultation:*

Cancer potency slope factors, and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHHA) using peer-reviewed scientific data for hundreds of compounds other than mineral spirits but comprising some components of mineral spirits. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public

notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further input is expected as the process moves forward.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

CAPCOA "Hot Spots" information does not include information for mineral spirits in ambient air. However, for some of its components, there are existing values which were developed in order to protect against perceptible occurrence of observable effects among an exposed human population for one-hour.

9. Key Risk Management Considerations:

The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in a screening risk assessment to determine the maximum offsite cancer risk for exposed human population. The process is not readily comparable to the air quality guideline approach to non carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control of volatile organic compounds, which are mineral spirit components. It appears that the options are under local control and are based on local risk, socioeconomic analyses and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Mineral spirits

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (DEP)

3. *Guideline Value(s):*

There are no specified Allowable Ambient Limits (AAL) or Threshold Exposure Limits (TEL) for mineral spirits by the DEP.

4. *Application:*

The guidelines are to be used mostly to assist in awarding permits, to verify compliance and enforcement and to be used as reference for regulatory actions. The guidelines consider the protection of public health and welfare irrespective of technological, economic and enforcement limitations. The selected chemicals were chosen as a representative sample in order to test and develop the proposed evaluation system. Health assessment of new chemicals is made on a case-by-case basis and using a standardized approach.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Key Reference(s):

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) Decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

6. *Peer Review Process and Public Consultation:*

The guidelines are not systematically peer-reviewed but are updated and modified by the DEP at a rate of 25 to 40 AALs per year and when revision is warranted. However, public consultation is solicited in public meetings and peer-reviews are organised.

7. Status of Guideline:

Mineral spirits is not on the list of chemicals to be evaluated.

8. Key Risk Assessment Considerations:

The Massachusetts system uses hazard assessment only and does not use the number of exposed individuals as a criterion for regulatory action except for prioritizing regulatory activities.

9. Key Risk Management Considerations:

The Department of Environmental protection believes that the evaluation system of AALS can minimize risks effectively while maintaining a practical regulatory approach to air toxics.

10. Multimedia Considerations of Guidelines:

The Massachusetts guidelines cover only ambient air but include a contribution factor of 20% in the establishment of Threshold Effect Exposure Limits (TEL). This factor assumes that 20% of the exposure is due to air for any given compound.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Mineral spirits. Specified as petroleum hydrocarbon materials: mineral spirits, heavy naphtha, hydrotreated heavy naphtha, hydrotreated middle distillate, hydrodesulfurized middle distillate, sweetened middle distillate, hydrotreated heavy naphthenic distillate, hydrotreated light distillate, naphtha heavy straight-run, naphtha, solvent naphtha light aliphatic, solvent naphtha medium aliphatic, stoddard solvent, VM & P naphtha.

2. *Agency:* Michigan State, Department of Environmental Quality (current) and Department of Natural Resources (previously)

3. *Guideline Value(s):*

The ambient impact of all petroleum hydrocarbon materials in this class must be below the initial threshold screening level (ITSL) of $3,500 \mu\text{g}/\text{m}^3$ developed by the Air Quality Division (AQD) of the Michigan Department of Environmental Quality, based on an 8 hour averaging time. This guideline originates from the NIOSH REL of $350,000 \mu\text{g}/\text{m}^3$ multiplied by a safety factor of 1%.

In addition, there are annual average ITSLs for several specific petroleum hydrocarbon solvent mixtures for which mixture-specific toxicological data were available, i.e.: $2 \mu\text{g}/\text{m}^3$ ITSL (annual average) for hydrotreated middle distillate, hydro-desulphurized middle distillate, sweetened middle distillate; $16 \mu\text{g}/\text{m}^3$ ITSL (annual average) for hydrotreated heavy naphthenic distillate; and $24 \mu\text{g}/\text{m}^3$ ITSL (annual average) for hydrotreated light distillate.

4. *Application:*

The guidelines are developed by the Toxics Unit of the Michigan Department of Environmental Quality for implementation of the Michigan's air toxic rules no. 230 and 232. The rules apply to new and modified processes for which an application for a permit is required and which emits toxic air contaminants.

5. *Documentation Available:*

Michigan Department of Environmental Quality, 1995/1997. Air Toxics Screening levels. Air Quality Division. 6 pp. + Appendices.

Key Reference(s):

Carpenter, C.P., et al., 1976. Petroleum hydrocarbon toxicity studies, XI. Animal and human response to vapors of deodorized kerosine. *Toxicol. Appl. Pharmacol.* 36:433-456.

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Vernot, E.H., Drew, R.T., Kane, M.L., 1990. Acute toxicological evaluation of hydrotreated naphthenic distillate. J. Amer. Coll. Toxicol., 1(2):133-134.

6. Peer Review Process and Public Consultation:

The guidelines are reviewed by the Toxics Unit upon requests for permits for certain compounds and information is based on latest review of the literature.

7. Status of Guideline:

Current and updated information according to Air Toxics Unit.

8. Key Risk Assessment Considerations:

The 8-hour ITSL value for aliphatic petroleum hydrocarbon solvents was developed based on the occupational limits specified by NIOSH and evaluation by the Air Quality Division.

9. Key Risk Management Considerations:

Risk assessment considers that for each source, the best available control technology should be used.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Mineral spirits

2. *Agency:* New Jersey Department of Environmental Protection

3. *Guideline Value(s):*

There is no recommended level in the New Jersey information document.

4. *Application:*

Not applicable.

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US ENVIRONMENTAL Protection Agency, Washington, DC.

6. *Peer Review Process and Public Consultation:*

The information is provided by New Jersey Department of Environmental Protection and Federal Standards and new evaluations are conducted by the risk management committee that evaluates the application to determine whether the source's permit should be approved.

7. *Status of Guideline:*

No guideline.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Mineral spirits

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

Mineral spirits are not currently specifically addressed under the guidelines from the New York State Air Guide (AG-1). However, New York State is considering adopting a Short-term Guideline Concentration (SGC; 1-h average air concentration) of 83,000 $\mu\text{g}/\text{m}^3$ and an annual Guideline Concentration (AGC) of 830 $\mu\text{g}/\text{m}^3$ (de Santis, 1997). The NIOSH value of 350,000 $\mu\text{g}/\text{m}^3$ is divided by 4.2 to obtain the AGC. The factor of 4.2 converts 40 hour work week to a continuous exposure. The general population is then no more exposed than workers.

Under section iv.A.2.c.1., for contaminants without numerical guidance, the contaminant must be limited to 0.1 $\mu\text{g}/\text{m}^3$ for moderate toxicity compounds and 1.0 $\mu\text{g}/\text{m}^3$ for low toxicity compounds. Stoddard solvent is a mixture and each component may have different effects. It cannot be classified directly in either of these categories, but is not a high toxicity compound because it is not listed as a carcinogen.

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate-to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

De Santis, S., 1997. Personal communication. New York State Department of Environmental Conservation (DEC)

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 pp. + Appendices.

Key Reference(s):

None.

6. Peer Review Process and Public Consultation:

The guidelines do not constitute a standard and are not peer-reviewed. The guidelines are updated by the NY Department of Environmental Conservation as new toxicological data are available and most guidelines are also updated based on changes in the occupational values. New chemicals are evaluated by the NY DEC on demand by the public.

7. Status of Guideline:

None yet. Annual and hourly guidelines will likely be set in April-May 1997.

8. Key Risk Assessment Considerations:

Chemical compounds are evaluated on whether they are of high, low, or moderate toxicity or high toxicity (carcinogens). But no risk assessment considerations for mineral spirits.

9. Key Risk Management Considerations:

Risk management is performed by monitoring by the source owner or his authorized agent and during selected sampling by DEC staff. Impact screening analyses used in the permitting process include a guide and a computer model described in the NY State guide.

10. Multimedia Considerations of Guidelines:

The NY guidelines cover only ambient air.

11. Other Relevant Factors:

Most of the values are based on the occupational exposure limits existing for a given compound.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical*: Mineral spirits.

2. *Agency*: World Health Organisation.

3. *Guideline Value(s)*:
No guideline.

4. *Application*:
No guideline applicable.

5. *Documentation Available*:
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organisation, Regional Office for Europe, Copenhagen, Denmark, 426 pp.

Key Reference(s):
WHO/Nordic Council of Ministers, 1985. Environmental Health Series No. 5: Chronic effects of organic solvents on the central nervous system and diagnostic criteria. WHO Regional Office for Europe, Copenhagen, Denmark, 274 pp.

6. *Peer Review Process and Public Consultation*:
None.

7. *Status of Guideline*:
No guideline.

8. *Key Risk Assessment Considerations*:
No risk assessment considerations, however, there has been some environmental criteria developed for the exposure to multiple organic solvents including white spirits (WHO, 1985).

9. *Key Risk Management Considerations*:
None.

10. *Multimedia Considerations of Guidelines*:
No information.

11. *Other Relevant Factors*:
No information.





11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Mineral spirits

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

Netherlands references comprise emission standards (1992) and environmental quality objectives (1994) or guidelines. The emission standard (1992) for mineral spirits falls under the emission standards for organic substances. Because mineral spirits are petroleum solvents containing hydrocarbons, they can be classified either under organic substances of class gO.2 or gO.3 for emissions in gaseous or vaporous form. For class gO.2, emissions standard is 100,000 µg/m³ for emissions with a mass flow of 2.0 kilograms per hour or more. For class gO.3, emissions standard is 150,000 µg/m³ for emissions with a mass flow of 3.0 kilograms per hour or more.

4. *Application:*

None.

5. *Documentation Available:*

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

The Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

Although it is said to largely occur in the case of probable carcinogenic substance, MAC (Maximum Acceptable Concentration at the workplace) values are not solely based on health consideration. In fact, national limit values include consideration of environmental, economic and social interests as well as technical options. Specific information on such details was not presented in the available documentation.

10. *Multimedia Considerations of Guidelines:*

No considerations for mineral spirits. However, multimedia exposure was not considered in the development of the current air limits for hydrocarbons. Inter-compartmental criteria which address this problem are being developed. A specific schedule for revisions based on this process has not been announced.

11. *Other Relevant Factors:*

No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Mineral spirits

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

None. According to Dr. K. Victorin (1997), no official Swedish air quality guideline was promulgated or will be in a near future for mineral spirits/Stoddard solvent.

4. *Application:*

Not applicable.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants: guideline values and conditions in Sweden. *Chemosphere* 27: 1691-1706.

Key Reference(s):

Victorin, K., 1997. Personal communication.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No official status but has been used as ad hoc basis by Swedish Regulators along with WHO guidelines.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.





11.10 Agency-Specific Summary: Federal of Government of Canada (CEPA)

1. *Name of Chemical:* Mineral spirits

2. *Agency:* Environment Canada and Health Canada

3. *Guideline Value(s):*

A revision is underway (PSL 2). However, mineral spirits is not on the list of substances under examination.

4. *Application:*

None.

5. *Documentation Available:*

Canadian Environmental Protection Act (CEPA), 1993-94. CEPA Priority Substance List (PSL 1).
Environment and Health Canada.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
μg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV *Threshold Limit Value* - an exposure concentration that should not induce an adverse effect in a work environment

TWA *Time-Weighted-Average* - allowable exposure averaged over an 8-hour workday or 40-hour work week

US EPA *United States Environmental Protection Agency*

WHO *World Health Organization*

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
PROPYLENE OXIDE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Propylene oxide was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing standard in 1984. A review of scientific and technical information relevant to setting an air quality standard for propylene oxide has previously been provided to stakeholders for comment. This document provides the rationale for recommending Ambient Air Quality Criteria (AAQC) and a half-hour Point of Impingement (POI) standard for propylene oxide.

Propylene oxide is a colourless, highly volatile organic liquid at ambient conditions. The vapour is highly flammable and can form an explosive mixture with air. Propylene oxide is mostly used as an intermediate in the chemical production of urethane foams, polypropylene glycol, and polyester fibres. Minor quantities are also used for the sterilization of medical equipment and for the fumigation of foodstuffs.

Propylene oxide is listed on Environment Canada's National Pollutant Release Inventory for facilities to report their releases to the environment. In 1993, five Canadian facilities reported a total atmospheric release of 60.68 tonnes of propylene oxide; all five sources were located in Ontario. These releases have been reduced substantially to about 11 tonnes since 1994 reporting year, and remained relatively consistent up to the 1997 reporting year. Air emissions accounted for all the releases reported in past years. Propylene oxide is not on the regular monitoring program in Canada. There is no current information available on the average ambient air levels of propylene oxide near Ontario facilities. There is also no average ambient air levels or background levels reported in the literature.

Humans can be exposed to propylene oxide through air, water, and food. Inhalation is the main route of human exposure. Effects observed in humans and experimental animals on short-term exposure include irritation of the eyes, skin, and respiratory system, as well as depression of the central nervous system. Although no data was available for humans, propylene oxide may have developmental and reproductive toxicity in some animal species.

Long-term exposure induces both cancer and non-cancer effects. Non-cancer effects in animals include inflammatory lesions of the lungs, damage to the respiratory system, and degeneration of nerve endings. Propylene oxide causes cell damage, thus stimulating cell division and tissue growth. It also binds to genetic material in cells. While both benign and malignant tumours have been observed at the site of exposure in several animal species, there is no reliable epidemiological study to provide evidence for an association between propylene oxide and human cancer incidence. Propylene oxide is classified

as a probable human carcinogen by the United States Environmental Protection Agency (US EPA) and a possible human carcinogen by the International Agency for Research on Cancer (IARC).

Ontario currently has a 24-hour average AAQC of $4,500 \mu\text{g}/\text{m}^3$ and an half-hour POI guideline of $13,500 \mu\text{g}/\text{m}^3$ for propylene oxide. These criteria were established in 1984 and were based on the adverse health effects of propylene oxide.

In revising the air quality standards for Ontario, the Ministry of the Environment is reviewing risk assessments and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Most of the agencies reviewed have developed criteria for propylene oxide based on the US EPA's chronic non-cancer Reference Concentration of $30 \mu\text{g}/\text{m}^3$ and/or derived from the US EPA's cancer risk estimates to obtain risk specific concentrations between 0.3 and $30 \mu\text{g}/\text{m}^3$, corresponding to lifetime additional cancer risk levels between one in a million and one in ten thousand, respectively. California is also proposing a short-term reference exposure limit of $6,100 \mu\text{g}/\text{m}^3$.

Of the criteria reviewed from the agencies, the Ministry has evaluated and accepted the scientific rationale and risk assessments developed by the US EPA and the State of California. As a result, the Ministry proposes to derive an annual AAQC based on the risk specific concentration of $0.3 \mu\text{g}/\text{m}^3$.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for propylene oxide:

- an annual average AAQC of $0.3 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide based on the carcinogenic effect of this compound; and,
- a 24-hour average AAQC of $1.5 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide based on the carcinogenic effect of this compound.

Based on the supporting science and dispersion modelling, a half-hour POI standard of $4.5 \mu\text{g}/\text{m}^3$ can be derived. Considering the magnitude of the reduction from the current POI guideline of $13,500 \mu\text{g}/\text{m}^3$ to the revised level of $4.5 \mu\text{g}/\text{m}^3$, meeting this proposed standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- **4.5 $\mu\text{g}/\text{m}^3$ to 450 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.**

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Propylene oxide was identified as a priority for review based on its pattern of use in Ontario, and recent toxicological information that has been published subsequent to the development of the existing standard. A review of scientific and technical information relevant to setting an ambient air quality standard for propylene oxide has previously been provided to stakeholders for their comments. This document therefore provides the rationale for recommending AAQC and a POI standard for propylene oxide.

2.0 General Information

2.1 Physical and Chemical Properties

Propylene oxide is a colourless, highly volatile liquid at ambient conditions. Its vapour is highly flammable and can form an explosive mixture with air. The substance may also polymerize violently and is very reactive with chlorine, ammonia, strong oxidants and acids. The following list provides some of its properties:

CAS #	75-56-9
RTECS #	TZ2975000
UN #	UN 1280
Conversion Factors	1 ppb = 2.37 $\mu\text{g}/\text{m}^3$ at 25°C and 101.3 kPa
Boiling Point	34.23 °C
Melting Point	-112.13 °C
Henry's Law Constant	
Flash Point	-19.44°C, closed cup
Specific Gravity	0.83 @ 20°C
Water Solubility	soluble in water
Log K_{ow}	
Formula	$\text{C}_3\text{H}_6\text{O}$
Molecular Weight	58.08
Vapour Density (air = 1)	
Vapour Pressure	445 mm Hg @ 20 °C
Common Synonyms	1,2-epoxypropane, methyl ethylene oxide, methyl oxirane, 1,2-propylene oxide

Its odour is described as ethereal, sweet, and alcoholic. The odour detection threshold for propylene oxide is 24,750 $\mu\text{g}/\text{m}^3$ (WHO, 1978; Ruth, 1986). The odour recognition threshold ranges from 80,000 to 470,000 $\mu\text{g}/\text{m}^3$, while odour irritation occurs at a significantly higher threshold of 1,125,000 $\mu\text{g}/\text{m}^3$.

2.2 Uses of Propylene Oxide

Propylene oxide is mostly used as an intermediate in the production of various chemicals such as polyurethane, polyester fibres, polypropylene glycol, glycol ethers, surfactants and lubricants (US EPA, 1985). Minor quantities of propylene oxide are also used for sterilisation of medical equipment and for fumigation of foodstuffs (IARC, 1994, WHO, 1978). The US Food and Drug Administration (cited in IARC, 1994) has approved the use of up to 25% propylene oxide in the production of food starch and has established regulations for use of propylene oxide in products in contact with food.

2.3 Sources and Levels

There are no data to indicate that propylene oxide occurs as a natural product. It enters the environment mainly through evaporation or in vented gases during production, handling, storage, transport and use. It is estimated that about 80% of the contribution to total propylene oxide exposure occurs through atmospheric releases. In addition to its direct release in air by chemical or manufacturing industries, propylene oxide may also originate from automobile exhaust and combustion exhausts of stationary sources that burn hydrocarbons. However, the major source of atmospheric pollution seems to be emissions through process vents. As waste gas is often removed by air scrubbing, and emissions from liquid wastes are controlled by incineration, it is estimated that only 0.1% of all propylene oxide used industrially may be lost to the atmosphere (US EPA, 1985;1987).

In 1993, the Canadian National Pollutant Release Inventory reported five emitters of propylene oxide which were all located in Ontario. Reported releases were exclusively to air. These emitters were manufacturing plants in the chemical and chemical products industries. Data regarding off-site transfers, such as recycling, reuse, recuperation, waste disposal and treatment, totalled 104.8 tonnes, indicating considerable use of propylene oxide in Ontario. The reported releases (60.9 tonnes) of 1993 decreased sharply in 1994 to 11.1 tonnes. Releases had remained consistent in 1995 (10.5 tonnes), 1996 (11.1 tonnes) and 1997 (13 tonnes) (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996, NPRI, 1997).

No information was available on ambient levels of propylene oxide in the literature. Propylene oxide has never been requested for survey, or monitored, in Ontario (MOE, 1997). The average ambient air levels near Ontario facilities are, therefore, unknown at the present time. From an analysis of applications for Certificates of Approval from 1986 to 1993 in Ontario, a sample of 3 sources of emissions of propylene oxide, covered by a Certificate, were identified. These certificates cover various chemical processing operations in the plants. The Ground Level Concentrations (GLC), predicted by Regulation 346 dispersion modelling for the three sources, range from $8.6 \times 10^{-6} \mu\text{g}/\text{m}^3$ to $817 \mu\text{g}/\text{m}^3$, with a median at $0.4 \mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

Propylene oxide can be formed in the photochemical smog cycle. The atmospheric chemical removal processes of propylene oxide include reactions with hydroxyl or other radicals, ozone, as well as photolytic transformation. Due to the high water solubility of propylene oxide, it can also be removed by precipitation. Propylene oxide is not expected to persist in air, as it has a half-life of up to 20 days (IARC, 1994). However, this half-life is long enough to subject propylene oxide to transboundary transport and to affect ecosystems following dry and wet deposition.

The estimated half-life for propylene oxide in freshwater is shorter than in air, up to 12.9 days (US EPA, 1985). In water, the degradation of propylene oxide is quicker than in air and it can be accelerated by the presence of chlorine. The partitioning of propylene oxide from water into sediments and its bioaccumulation in biota are unlikely to be significant. Even though propylene oxide is highly soluble in water, it also evaporates to a greater extent from water bodies than soil.

Pertinent data regarding the fate and transport of propylene oxide in soil are limited. The microbial degradation is possible by properly acclimatized microorganisms. The significance of transport of propylene oxide in soils is uncertain, but its aqueous hydrolysis in moist soils has been shown to be significant, hence reducing the possibility of leaching in wet conditions. Propylene oxide can also evaporate rapidly from dry soils.

3.0 Toxicology of Propylene Oxide

Inhalation is the main route of propylene oxide exposure in humans. Inhaled propylene oxide is readily absorbed, distributed throughout the body, and rapidly metabolised (IARC, 1994). Allergic contact dermatitis develops following dermal exposure to propylene oxide. No data were found on the effect of ingestion of this compound in humans.

3.1 Acute Toxicity - Inhalation

The acute effects of propylene oxide include irritation of the eyes, skin and respiratory tract. It is reported to be a mild central nervous system depressant in humans, and can produce a lack of coordination, ataxia, and general depression (IARC, 1994). Exposure of animals (such as rodents and dogs) to propylene oxide resulted in eye and nose irritation, nasal discharge, injury to the respiratory tract and depression of the central nervous system; the severity of which increased with increasing level and length of exposure. The lowest lethal concentration for 4-hour exposures is approximately 5,250 mg/m³ for rats and 900 mg/m³ for mice (reviewed in WHO, 1985; US EPA, 1987; IARC, 1994). Data from a National Toxicology Program (NTP) study in which mice exposed to 387, 859, up to

2,970 ppm propylene oxide for 4 hours indicated dose-related mortality at the higher exposures (NTP, 1985 as cited in OEHHA, 1998). No gross abnormalities were noted at the lower doses. A lowest-observed-adverse-effect level (LOAEL) of 387 ppm (921 mg/m³) for mild adverse effects (irritation of the nose) was established.

3.2 Subchronic/Chronic Toxicity - Inhalation

The predominant long-term exposure effects may include adverse effects on the nervous system, irritation of the nose and other respiratory passages, including lung damage. Rats exposed to propylene oxide above 119 mg/m³ (50 ppm) for up to 4 weeks developed hypoactivity, respiratory epithelial hyperplasia, degeneration of olfactory epithelium, and cell proliferation at both sites (Eldridge *et al.*, 1995). These effects were found to be dose- and time-dependent, and were reversible upon cessation of exposure. Exposure to a high concentration of propylene oxide (3,555 mg/m³, 1500 ppm) for 6 hours per day, 5 days per week for 7 weeks, revealed degeneration of nerve endings in both the central and peripheral nervous systems of the rats, partly manifested as awkward movement of the hindlegs (Ohnishi *et al.* 1988; Ohnishi and Murai, 1993). Lifetime inhalation studies in laboratory animals have indicated that propylene oxide may cause inflammatory lesions of the lungs, nasal cavity, and trachea, lowered body weights, increased degenerative changes of nasal mucosa, and mortality increase in rats (Kuper *et al.*, 1988).

3.3 Reproductive/Developmental Toxicity

No data was available for humans, but in some animal species, propylene oxide may cause developmental and reproductive toxicity. In rats exposed to 188 mg/m³, there was a significant decrease in maternal body weight gain, some evidence of embryo toxicity (increased resorption and decreased number of corpora lutea, implants, and live fetuses), as well as decreased foetal body weights and crown-to-rump length, and delayed ossification (Hackett *et al.* 1982; Hardin *et al.* 1983). The only signs of maternal toxicity in rabbits exposed to the same level of propylene oxide were a decrease in maternal body weight gain (Hackett *et al.* 1982; Hardin *et al.* 1983). Monkeys exposed to propylene oxide for two years showed decreased sperm counts and motility at 240 and 710 mg/m³ (Lynch *et al.* 1984a).

3.4 Genotoxicity

Like other epoxides, propylene oxide is DNA-reactive, since it binds covalently to DNA to form DNA adducts in various organs of mice, rats and dogs (Segerbäck *et al.* 1994; IARC, 1994). It was found to be a direct-acting mutagen in a variety of bacteria, fungi and yeast test systems and caused sex-linked recessive lethal mutations in *Drosophila melanogaster* (IARC, 1994; US EPA, 1997). Propylene oxide induced mutation, chromosomal aberrations and sister chromatid exchange in

mammalian cells *in vitro* as well as, chromosomal aberrations and sister chromatid exchange in human peripheral blood lymphocytes (IARC, 1994; US EPA, 1997). DNA repair activity was initiated by propylene oxide in the lymphocytes of occupationally exposed workers (Pero *et al.* 1982). Propylene oxide has also been reported to induce oncogenic transformation in Syrian hamster embryo cells by adenovirus SA7 (Calabrese and Kenyon, 1991). Evidence of mutagenicity following *in vivo* exposure is inconclusive.

3.5 Carcinogenicity

The available toxicological data regarding propylene oxide indicates that the compound is a contact carcinogen in rodents, causing forestomach tumours following ingestion (Dunkelberg, 1982), nasal and mammary tumours after inhalation exposure (Lynch *et al.* 1984b; Renne *et al.* 1986), and subcutaneous tumours after subcutaneous injection (Walpole, 1958; Dunkelberg, 1981). There was no reliable epidemiological study which could provide evidence for an association between propylene oxide and human cancer incidence. Several retrospective cohort studies (Hogstedt *et al.* 1979, 1986, 1988; Thiess *et al.* 1981; Gardner *et al.* 1989) and a case-control study (Ott *et al.* 1989) showed that there was no significant increase in cancer mortality due specifically to propylene oxide exposure. Therefore, International Agency for Research in Cancer (IARC, 1994) has classified propylene oxide as possibly carcinogenic to humans (group 2B), given inadequate proof of carcinogenicity in humans and sufficient proof in experimental animals. It is also considered a probable human carcinogen (group B2) under the United States Environmental Protection Agency (US EPA, 1997) weight-of-evidence classification system, based on inadequate human data and an increased incidence of benign and malignant tumours in two animal species.

3.6 Environmental Effects

No data were found on the effects of propylene oxide on terrestrial wildlife. Propylene oxide appears to be moderately toxic to aquatic organisms, as 96-hour LC₅₀ values for fish range from 141 mg/L for mosquito fish (*Gambusia affinis*) to 215 mg/L for bluegill sunfish (*Lepomis macrochirus*) (Environment Canada, 1985).

4.0 Existing Ambient Air Quality Criteria

4.1 Overview

The current ambient air quality criterion (AAQC) for propylene oxide in Ontario was set in 1984. The AAQC is currently set at $4,500 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time and the half-hour point of impingement (POI) guideline is set at $13,500 \mu\text{g}/\text{m}^3$ (MOEE, 1994a).

The basis for air quality guidelines and standards developed by the following agencies have been reviewed: US EPA, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Agency-specific summaries of information concerning air quality guidelines for propylene oxide are presented in Section 11.0 of this report. A brief summary is presented in Table 1.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations, to half-hour POI standards and, a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Existing air quality criteria have been based on both non-carcinogenic endpoints and carcinogenic endpoints. Most of the U.S. state agencies have established their annual or lifetime guidelines from either the US EPA Reference Concentration (RfC) of $30 \mu\text{g}/\text{m}^3$, which is for the protection of the upper respiratory system from chronic inhalation exposures, or the US EPA inhalation cancer unit risk estimates for lifetime exposures based on a carcinogenicity assessment (at risk specific exposure concentrations between $0.3 \mu\text{g}/\text{m}^3$ to $30 \mu\text{g}/\text{m}^3$ for a lifetime, representing estimated additional cancer risk of one in a million to one in ten thousand, respectively). The states of California (OEHHA, 1997) and New Jersey adopted the US EPA's RfC for their annual criteria, whereas Michigan has adopted the RfC for its 24-hour air quality criterion. The states of California, Massachusetts and Michigan adopted the risk-specific concentration of $0.3 \mu\text{g}/\text{m}^3$ for a cancer risk level of one in a million from the US EPA as their annual criteria.

New York State's current air guidelines were derived from occupational exposure limits developed by the American Conference of Governmental Industrial Hygienists (ACGIH). However, New York State is expected to revise its annual average guideline based on the US EPA inhalation unit risk for lifetime

exposure (deSantis, 1997). The Netherlands has specified a target limit of $1 \mu\text{g}/\text{m}^3$, based on an estimated additional risk of cancer of one in a million.

The State of Massachusetts has a short-term (24-hour) guideline of $6 \mu\text{g}/\text{m}^3$, derived from the non-cancer RfC of the US EPA, taking into account that inhalation represents 20 % of exposure from all media. The State of New York based its one-hour average concentration on worker exposure limits. The Office of Environmental Health Hazard and Assessments (OEHHA) of the California Environmental Protection Agency has recently proposed to revise its one-hour acute reference exposure level from $1,000 \mu\text{g}/\text{m}^3$ to $6,100 \mu\text{g}/\text{m}^3$. This level has been established for the mild irritation effects of propylene oxide in mice based on a NTP (1985) short-term inhalation animal study (OEHHA, 1998).

No guidelines were found for WHO, Sweden or the Federal Government of Canada.

Table 1. Summary of Existing Air Quality Guidelines¹ for Propylene oxide

Agency	Guideline Value	Basis of Guideline	Date ²	Comments
US EPA	30 µg/m ³	Reference concentration (RfC) - nest-like infolds - nasal respiratory epithelium	1990	Non-cancer endpoint - LOAEL (HEC) adjusted with uncertainty factors 2-yr rat inhalation study
	0.3 µg/m ³ (lifetime exposure)	Inhalation unit risk	1985	1 * 10 ⁻⁴ additional cancer risk
	3 µg/m ³ (lifetime exposure)	3.7 * 10 ⁻⁴ per (µg/m ³)		1 * 10 ⁻⁵ additional cancer risk
	30 µg/m ³ (lifetime exposure)	Haemangiomas and hemangiosarcomas of mouse nasal turbinates		1 * 10 ⁻⁴ additional cancer risk
California (CAPCOA)	30 µg/m ³ (annual)	US EPA RfC	1993	Non-cancer endpoint - inhalation reference concentration
	0.3 µg/m ³ (lifetime exposure)	based on US EPA unit risk 3.7 * 10 ⁻⁴ per (µg/m ³)	1988	Proposition 65 carcinogen; risk specific concentration at 1 * 10 ⁻⁴ risk
	1,000 µg/m ³ (1-hour average)	Central nervous system effects	1993	4-hour inhalation mouse study (NTP 1985)
Massachusetts	0.3 µg/m ³ (annual average)	US EPA unit risk 3.7 * 10 ⁻⁴ per (µg/m ³)	1995	Carcinogenic endpoint - inhalation
	6 µg/m ³ (24-hour average)	US EPA RfC	1995	Threshold effects exposure limit (TEL)
Michigan	30 µg/m ³ (24-hour average ITSL)	US EPA RfC	1996	Non carcinogenic endpoint - inhalation reference concentration
	0.3 µg/m ³ (Annual IRSI; lifetime exposure)	US EPA unit risk 3.7 * 10 ⁻⁴ per (µg/m ³)	1996	Annual IRSI (Initial risk screening level): 1 * 10 ⁻⁴ additional cancer risk
	3 µg/m ³ (SRSL; lifetime exp.)			SRSL: 1 * 10 ⁻⁵ additional cancer risk
New Jersey	30 µg/m ³ (Maximum annual exposure)	US EPA RfC	1994	Non-cancer endpoint - inhalation reference concentration
New York	110 µg/m ³ (annual) AGC to be revised to 0.3 µg/m ³	Occupational US EPA RfC	1991	Derived from ACGIH TLV-TWA DeSantis (1997)
	11,000 µg/m ³ (hourly) SGC	Occupational	1991	Derived from ACGIH TLV-TWA
WHO	none		1987	No value found
The Netherlands	1 µg/m ³ (target value/annual average)		1987	1 * 10 ⁻⁴ additional cancer risk
Sweden	none		1993	No value found
Canada	none		1993	Not evaluated
Ontario	4,500 µg/m ³ (24-hour average)	Health	1984	Ambient Air Quality Criteria
	13,500 µg/m ³ (half-hour POI)	Health	1984	Point of Impingement (interim standard)

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

4.2 Evaluation of Existing Criteria

When Ontario proposed its criteria for propylene oxide in 1984, only limited toxicological data was available. A LOAEL of 464,000 $\mu\text{g}/\text{m}^3$, based on slight increase in the lung weight of female guinea pigs was used. A safety factor of 100 was applied to the LOAEL to obtain the 24 hour-average AAQC for the protection of human health (MOE, 1984). The evidence of propylene oxide-induced carcinogenicity in animals, and the classification of this compound as a probable or possible carcinogen by some agencies, would indicate that the carcinogenicity endpoint should be considered in the development of air quality standards for propylene oxide.

With the exception of The Netherlands and New York, the agencies reviewed developed their limits based on the US EPA assessments for non-carcinogenic risk and/or carcinogenic risk. The State of California has derived an acute reference exposure level (REL; 1-hour averaging) of for propylene oxide based on data from a mouse inhalation study.

Since inhalation of propylene oxide leads to degeneration and hyperplasia of the nasal and olfactory tissues, and induces tumour formation in respiratory tissues, these two effects should be characterized in order to provide the most appropriate rationale for the development of air quality standards for Ontario.

US EPA Carcinogenic Risk Assessment

The US EPA (1985) has conducted a cancer risk assessment based on the two-year NTP inhalation study (NTP, 1985; Renne *et al.* 1986). Groups of 50 male and female F344 rats and B6C3F₁ mice were exposed to propylene oxide by inhalation at 0, 475 or 950 mg/m^3 (0, 200, 400 ppm) for 6 hours/day, 5 days/week, for 103 weeks. Tumours were observed in the nasal cavity of both rats and mice at the highest dose. However, only the mice showed a statistically significant increase in incidence over the controls. Therefore, the mouse data were used to derive the dose response relationship at low doses in humans. The unit carcinogenic risk from inhalation exposure was estimated to be 3.7×10^{-6} per ($\mu\text{g}/\text{m}^3$) in humans.

The derivation of the unit risk for propylene oxide was based on several assumptions. The cancer effect was assumed to be a non-threshold phenomenon, and that any dose, no matter how small, would lead to some risk. The dose response relationship at low doses was assumed to be linear and was obtained by extrapolating tumour response from high doses using the linearized multistage model. The carcinogenic potency for humans, expressed as the cancer slope factor at low dose, was extrapolated from the potency in mice, assuming that the toxicant was equipotent in animals and humans, is expressed as mg per kg of body weight per day.

The NTP study was a well conducted study with an adequate number of animals of both sexes treated for a lifetime. The route of exposure was relevant and a thorough histopathological examination was performed. The major concerns, if any, about the cancer unit risk lie with the risk assessment

approach, specifically dealing with issues related to treating propylene oxide carcinogenicity as a non-threshold phenomenon, high to low dose extrapolation, as well as rodent-to-human extrapolation

Threshold versus Non-threshold

In the NTP study, mice were administered propylene oxide at dose levels of 0, 475 and 950 $\mu\text{g}/\text{m}^3$. Only animals in the highest dose group had significantly elevated incidences of nasal tumours. For example, in male mice, haemangiomas: 0/50, 0/50, 5/50 and haemangiosarcomas: 0/50, 0/50/ 5/50 for the three corresponding dose groups; and in female mice, the combined haemangiomas and haemangiosarcomas: 0/50, 0/50/ 5/50 in the three corresponding dose groups. The low dose group did not show any tumours. The response therefore appears to have a threshold with no cancer development at the low dose level (475 mg/m^3) and a 20% response at the high dose (950 mg/m^3). At the same time, nasal cavity inflammation and epithelial hyperplasia were increased in animals at both the low and high doses. While a no-observed-adverse-effect level (NOAEL) has not been found in the long-term studies, a NOAEL has been identified at 119 mg/m^3 (50 ppm) for propylene oxide-induced cell injury and proliferation in the respiratory and nasal epitheliums on short-term (4-week) exposure (Eldridge *et al.* 1995). The observation of a steep inclination of the dose-response curve for tumour formation, and the presence of cell injury and proliferation in the same target tissues, suggest a strong cytotoxic and proliferative component in the mechanism of propylene oxide carcinogenicity (i.e. propylene oxide acts as a promoter) at the high dose.

On the other hand, propylene oxide is a known genotoxic agent and mutagen based on *in vitro* studies, and has been shown to interact with DNA *in vivo*. Therefore, propylene oxide is likely an initiator, or in other words (or more specifically), a toxicant that causes neoplastic cell transformation by inducing mutation or DNA lesion through direct interaction with DNA. While a threshold may exist for non-genotoxic carcinogens, such as promoters, the carcinogenic outcome is probabilistic in nature for initiators and no threshold is expected. Cancer induction by propylene oxide at levels above the cell proliferation threshold may involve both mechanisms, genotoxic effect and cell proliferation, probably acting synergistically. However, even if propylene oxide is present only at low concentrations, it can potentially act as an initiator, and the presence of another cell proliferator (which is often present in the environment) would allow the expression of propylene oxide-induced mutagenic events. Therefore, it is not unreasonable to assume a non-threshold phenomenon in determining the dose-response relationship at low doses for propylene oxide carcinogenicity, particularly because carcinogenic thresholds cannot be determined based on experimental observation only (reviewed by Zeise *et al.* 1987; Purchase and Auton, 1995). The selection of risk assessment methodology (threshold versus non-threshold) has to be based on an understanding of the mechanism of toxicity (Purchase and Auton, 1995).

High-to-Low Dose Extrapolation

The dose response curve was not adequately delineated experimentally in the NTP mouse study because propylene oxide was administered at two different dose levels only and only animals at the

highest dose showed a relatively high incidence of tumours. The steep inclination of the dose response curve is consistent with other DNA-reactive nasal carcinogens that are both weak initiators and strong promoters, such as formaldehyde (Kerns *et al.* 1983; Monticello *et al.* 1996) and methyl sulphate (Frame *et al.* 1993). For this type of carcinogen, the nonlinear dose-response relationship can only be adequately modelled using a biologically based model, such as the type developed by Moolgavkar and Knudson (1981). However, a lack of definitive mechanistic data does not allow this type of model to be applied. Considering the genotoxic effects of propylene oxide, a linearized multistage model was used. The use of this model was based on the assumption that the carcinogenic effects of genotoxic carcinogens were linearly dose-related. However, the extrapolation of responses from the single high dose of the NTP mouse data to low doses, without knowledge of the responses at intermediate doses likely results in an overestimation of the carcinogenic risk at low environmental levels.

Rodent-to-Human Extrapolation

In the US EPA risk assessment, surface-based extrapolation of the administered/absorbed dose has been used to determine the human equivalent dose from cancer data obtained in rodents. Interspecies conversion is done on the basis of basal energy metabolism which is approximated by the surface area of a hypothetical spherical animal (Krewski *et al.* 1990). The basis of the extrapolation lies with the empirical observation that metabolic rate shows a better correlation with surface area than with body weight. Based on this, the assumption is that a similar relationship will exist for various toxicological effects (Davidson *et al.* 1986). This assumption is supported by Freireich's (1966) study of anticancer agents using a number of different animal species, including man. However, there is an appreciable uncertainty associated with extrapolation methods based on either body weight or surface area (reviewed in Kreswki *et al.* 1990). The choice of a suitable extrapolation method may depend on the individual chemical.

Another approach to species extrapolation assumes that toxic response results from tissue exposure to toxic chemicals, and that a particular tissue dose induces the same intensity of response in all mammalian species, including humans. Premised on this assumption, Segerbäck and coworkers (1994) measured the *in vivo* levels of haemoglobin-propylene oxide adduct, and DNA adduct, in various organ tissues in an attempt to evaluate whether tissue dose is correlated to surface area of the exposed animal through inhalation. The experimental results indicated that the propylene oxide tissue dose in the various organs, examined per mg per kg body weight administered or absorbed, was virtually the same in the three investigated animal species (mouse, rat and dog) and was not related to the surface area of the animal. The expected haemoglobin adduct level in man, based on body weight extrapolation from animal data, agreed with the estimated adduct level in propylene oxide exposed workers. On the other hand, extrapolation based on surface area overestimated the adduct levels. Based on their findings, Segerbäck and coworkers (1994) concluded that species extrapolation based on body weight was more consistent with the existing pharmacokinetic information on propylene oxide. Using this method, the carcinogenic potency factor for propylene oxide, as derived by US EPA, would be revised downward by a factor of 10.

While pharmacokinetics may account for part of the difference in the severity of toxic response in different species, there could be some inherent biological factors that make some species more sensitive than others to the effects of a toxicant. Therefore, the same toxicant level in the target organ may not elicit the same level of response in different animal species. These pharmacodynamic factors are not known for propylene oxide and remain a source of uncertainty for the cancer potency estimate for humans, even if pharmacokinetic information has been considered in interspecies extrapolation.

US EPA Noncarcinogenic Risk Assessment

The US EPA (1997) inhalation reference concentration (RfC) of $30 \mu\text{g}/\text{m}^3$ was calculated on the basis of a 2-year rat chronic propylene oxide inhalation study conducted by Kuper *et al.* (1988). Wistar rats of both sexes were exposed to 0, 71, 238 or $713 \text{ mg}/\text{m}^3$ (0, 30, 100 or 300 ppm) propylene oxide through inhalation. Survival of the rats in the three exposed groups was adversely affected. Incidences of several non-neoplastic degenerative and hyperplastic nasal injuries increased significantly in all exposed groups. However, nest-like infold of the respiratory epithelium, in both males and females, was the only statistically significant effect noted in animals exposed to the low dose ($71 \text{ mg}/\text{m}^3$), and was seen only in rats exposed for 28 months. This study identified the Lowest-Observed-Adverse-Effect Level (LOAEL) for extra thoracic respiratory effects at a concentration of $71 \text{ mg}/\text{m}^3$ (30 ppm). The LOAEL human equivalent, LOAEL(HEC), was estimated to be $2.9 \text{ mg}/\text{m}^3$. Application of uncertainty factors to the LOAEL(HEC) (3 for interspecies extrapolation, 3 for the use of a LOAEL associated with a mild effect, and 10 for the protection of sensitive human sub-populations) resulted in a RfC of $30 \mu\text{g}/\text{m}^3$.

The Kuper study (1988) was a long-term, well-conducted study with a large number of animals. All critical effects had been examined using sensitive techniques, and at multiple durations and exposure levels. The only drawback is that the study failed to identify a NOAEL. As a result, US EPA has only medium confidence in this RfC. Nevertheless, there are several other chronic inhalation studies (NTP, 1985; Lynch, *et al.* 1984b) and inhalation developmental studies (Hackett *et al.* 1982; Hardin *et al.* 1983) that also corroborate this result.

Other non-threshold derivations

The State of California has extrapolated data from a 4-hour mouse study, to derive an acute REL of $6,100 \mu\text{g}/\text{m}^3$ for mild irritation effects in the nose. The LOAEL of 387 ppm for a 4-hour exposure was converted to a LOAEL for a 1-hour exposure. An uncertainty factor of 300, resulting from a factor of 3 for the use of a LOAEL, 10 for interspecies extrapolation and 10 for sensitive individuals, was then applied to the 1-hour LOAEL of 774 ppm ($1844 \text{ mg}/\text{m}^3$). The State of Massachusetts derived its 24-hour TEL of $6 \mu\text{g}/\text{m}^3$ from the US EPA RfC of $30 \mu\text{g}/\text{m}^3$. This revised value took into account for multimedia exposure (20% from air exposure).

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including propylene oxide, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards; and, the appropriateness of considering the carcinogenicity of propylene oxide as the most sensitive endpoint and technical or economic impacts that may be anticipated consequent to the revision of the air quality standards.

During the consultation period, no comments were received from the industrial sectors or the general public regarding propylene oxide.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments on the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard, which are presented in Section 8.0 below. This step represents the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the level of the air quality standard for propylene oxide. If the proposed standard cannot be met immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In the meantime, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds. For instance, where there is a greater than 10-fold difference between the revised health-based values and the current standard, an interim standard may be warranted, depending on the extent of risk management analyses.

7.0 Considerations in the Development of Air Quality Standards for propylene oxide

The current Ontario 24-hour AAQC of 4,500 $\mu\text{g}/\text{m}^3$ for propylene oxide was set in 1984. The half-hour POI guideline was set at 13,500 $\mu\text{g}/\text{m}^3$.

Exposure to propylene oxide may induce irritation to the eyes, skin, and the respiratory tract. Inhalation of this compound may result in mild central nervous system depression. In animals, long-term exposure to propylene oxide leads to degeneration and hyperplasia of the nasal and olfactory tissues. In addition, lifetime exposures of rodents to propylene oxide resulted in elevated incidence of nasal cancer, tumours in the thyroid gland and other tissues. Based on the induction of lesions in nasal tissues following exposure to propylene oxide, the US EPA has developed a non-cancer inhalation RfC of $30 \mu\text{g}/\text{m}^3$. The US EPA has also estimated that lifetime exposure to propylene oxide at $0.3 \mu\text{g}/\text{m}^3$ may result in an increase in cancer incidence at a risk level of one in a million. Most of the U.S. agencies studied have adopted both of the non-cancer criterion and the cancer unit risk estimate of the US EPA for their air quality criteria derivation.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide and the science upon which these standards are based. Of the criteria reviewed, the Ministry has evaluated and accepted the scientific rationale and risk assessments developed by the US EPA and the State of California. The Ministry accepts that there is a certain level of uncertainty underlying the carcinogenicity of propylene oxide, particularly with respect to the lack of epidemiological evidence, and the possible overestimation of risk introduced in the extrapolation of low dose responses from animal species to humans. However, the potential carcinogenic effect of this compound cannot be ruled out.

In general, the Ministry strives to manage exposure to carcinogens down to a risk represented by no more than 1 excess cancer in 1,000,000. This is consistent with the Ministry's approach to carcinogenic risk management for other environmental exposures (e.g., in drinking water and for contaminated sites) and with other jurisdictions, in particular throughout the United States. As a result, the Ministry proposes to derive an annual AAQC based on the risk specific concentration of $0.3 \mu\text{g}/\text{m}^3$.

The Ministry of the Environment normally uses a factor of 15 to derive half-hour POI standards from criteria based on annual average concentrations and a factor of 5 to derive 24-hour AAQC from criteria based on annual average concentrations. These factors are derived from empirical measurements which ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b).

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criteria for propylene oxide:

- an annual average AAQC of $0.3 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide based on the carcinogenic effect of this compound; and,

-
- a 24-hour average AAQC of $1.5 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide based on the carcinogenic effect of this compound.

Based on the supporting science and dispersion modelling, a half-hour POI standard of $4.5 \mu\text{g}/\text{m}^3$ can be derived. Considering the magnitude of the reduction from the current POI guideline of $13,500 \mu\text{g}/\text{m}^3$ to the revised level of $4.5 \mu\text{g}/\text{m}^3$, meeting this proposed standard immediately may not be possible due to implementation issues related to economic/technical feasibility and the required timeframe to establish appropriate emission control technology.

In light of these potential concerns, the Ministry is proposing to determine an interim POI standard from the following range of values:

- $4.5 \mu\text{g}/\text{m}^3$ to $450 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for propylene oxide; these concentrations are equivalent to risk levels of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime, respectively.

The proposed final POI standard will be the lower number of the range from which the interim standard is selected. The establishment of an interim standard is considered an initial step in a scheduled reduction process over an achievable timeframe to the final standard. Details of the reduction process will be discussed with stakeholders as a part of a detailed risk management plan. The interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all

other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for propylene oxide can be sent to:

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Ontario Ministry of the Environment
135 St. Clair Ave West
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Fax: 416 327-2936
e-mail: sdb-eb@ene.gov.on.ca

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Propylene oxide

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. The reference concentration for chronic inhalation exposure (RfC) calculated on the basis of a chronic 2-year rat study is listed as $30 \mu\text{g}/\text{m}^3$ in the IRIS database (US EPA, 1997; last review 08/15/94). Propylene oxide is classified as a probable human carcinogen (B2) with a unit risk from inhalation exposure of 3.7×10^{-6} per $\mu\text{g}/\text{m}^3$.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

US EPA, 1985. Health and Environmental Effects Profile for Propylene Oxide. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment Office of Research and Development, US Environmental Protection Agency, Cincinnati, OH. EPA/600/X-85/401.

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6. Peer Review Process and Public Consultation:

US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the assessment for each chemical listed in IRIS have undergone extensive internal and external scientific and policy reviews. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:

No current guidelines exist for propylene oxide.

8. Key Risk Assessment Considerations:

The US EPA (1997) has calculated an RfC which is "an estimate of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" for adverse effects other than cancer. This RfC was calculated based on a 2-year rat inhalation study (Kuper *et al.* 1988). Rats were exposed to 0, 71 mg/m³, 280 mg/m³ or 713 mg/m³ (0, 30, 100, 300 ppm) of propylene oxide for 6 hours/day, 5 days/week for 123 weeks for females and 124 weeks for males, respectively. Survival was adversely affected by exposure to propylene oxide. By week 115, there was a statistically significant increase in mortality in rats of both sexes exposed to 713 mg/m³. A human equivalent concentration of the frank effect level, FEL (HEC), of 127 mg/m³ was established. Slight nest-like infolds of the respiratory epithelium in both males (18, 24, and 28 months) and females (24 and 28 months) was the only statistically significant effect in the animals exposed to 71 mg/m³ and was seen only in rats exposed for 28 months. This study identified a lowest adverse effect level (LOAEL) for extra thoracic respiratory tract effects at a concentration of 71 mg/m³. The human equivalent concentration of the lowest adverse effect level, LOAEL (HEC), was determined to be 2.9 mg/m³ (2,900 µg/m³).

An uncertainty factor of 100 was applied to the LOAEL (HEC) to account for intraspecies variability (i.e. to protect sensitive individuals, UF = 10), to account for interspecies extrapolation and for the use of a LOAEL when the effect was mild (UF = 10). As a result, the RfC was determined to be 30 µg/m³.

Carcinogenicity unit risk from inhalation exposure was calculated from the NTP (1985) and Renne *et al.* (1986) animal studies. The NTP studies exposed both F344/N rats and B6C3F1 mice (50/sex/dose) to 0, 475 or 950 mg/m³ (0, 200, 400 ppm) propylene oxide by inhalation 6 hours/day, 5 days per week for 103 weeks. Tumours were observed in various organ tissues, however, only nasal cavity tumours were considered by NTP as treatment-related. Although both rats and mice developed nasal cavity tumours at the highest dose, only the mice showed a statistically significant increase in incidence over the controls. Therefore only the mouse data were used to derive the dose response relationship at low doses in humans. The unit carcinogenic risk from inhalation exposure was estimated to be 3.7×10^{-6} per $\mu\text{g}/\text{m}^3$ in humans.

Transformed animal doses were calculated assuming a 50% pulmonary absorption, and an exposure duration of 103 weeks. The 50% absorption assumption is consistent with the absorption efficiency observed for epichlorohydrin in the respiratory tract of rats (Stott and McKenna, 1984). The experimental data using the transformed animal dose levels were fitted to the linearized multistage model, in estimating the animal slope factor at low dose levels. The animal cancer slope factor was estimated at 9.8×10^{-1} per ($\mu\text{g}/\text{kg}$)/day. Assuming body surface area equivalency, the human slope factor was determined to be 13 per ($\mu\text{g}/\text{kg}$)/day using an animal body weight of 0.03 kg, a human body weight of 70 kg and animal lifespan of 103 weeks.

9. Key Risk Management Considerations:

None, since no guidelines for ambient air exist.

10. Multimedia Considerations of Guidelines:

The oral drinking water unit cancer risk for propylene oxide is reported at 6.8×10^{-6} $\mu\text{g}/\text{L}$. The oral slope factor was calculated as 2.4×10^{-1} per (mg/kg)/day.

11. Other Relevant Factors:

No information.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Propylene oxide

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The non-cancer reference exposure level (REL) for chronic inhalation is $30 \mu\text{g}/\text{m}^3$ and has been adopted from the US EPA RfC. Propylene oxide is listed as a substance requiring the calculation of annual average concentration. Chronic exposure reference levels should be compared with modelled annual average air concentrations. The unit risk, as shown in US EPA IRIS is listed as 3.7×10^{-6} . An acute inhalation REL of 6,100 is being proposed.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessment. These guidelines are prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider reference exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

5. *Documentation Available:*

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

NTP (National Toxicology Program), 1985. Toxicology Studies of Carcinogenesis of Propylene Oxide (CAS No. 75-56-9) in F344/N rats and B6C3F1 mice (inhalation studies). NTP Tech. Rep. Ser. No 267, NTP, Research Triangle Park, NC, NIH Publ. No. 85-2527.

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OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Propylene Oxide. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California.

Risk Assessment Advisory Committee, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines.

Key Reference(s):

US EPA, 1997. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

The guideline is current.

8. Key Risk Assessment Considerations:

California has adopted the EPA's RfC of $30 \mu\text{g}/\text{m}^3$ as its non-cancer Reference Exposure Level (chronic) (OEHHA, 1997). Propylene oxide is also listed as a substance whose emissions must be quantified. It is considered a substance for which annual average concentration should be calculated.

A proposed acute reference ambient level acceptable for 60 minute exposures to propylene oxide is $6,100 \mu\text{g}/\text{m}^3$. The acute acceptable reference level was derived from the NTP (1985) mouse study which established a LOAEL of 387 ppm for dyspnea (considered a mild irritation effect). An extrapolated 774 ppm 1-hour concentration was divided by an uncertainty factor of 300: 3 for the use of a LOAEL, 10 for interspecies variation, and 10 for intraspecies variation (OEHHA, 1998).

9. Key Risk Management Considerations:

The exposure guidelines were prepared for both non-cancer and cancer endpoints. The cancer-based value is used in a screening risk assessment to determine the maximum offsite cancer risk for exposed human population. The process is not readily comparable to the air quality guideline approach to non-

carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses, and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993).

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Propylene oxide

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL; 24-hour average) for propylene oxide is $6 \mu\text{g}/\text{m}^3$ and the Allowable Ambient Limit (AAL; annual average) is $0.3 \mu\text{g}/\text{m}^3$ corresponding to an excess lifetime cancer risk of 1×10^{-6} .

4. *Application:*

"... The Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) decisions made by ORS regarding some discrepancies observed in the RFC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Key Reference(s):

US EPA, 1983. Health assessment document for propylene oxide. EPA-600/8-82-007 F. EPA, ORD, OHEA, Washington, DC.

US EPA, 1994. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

American Conference for Governmental Industrial Hygienists (ACGIH). 1986. Documentation of the Threshold Limit Values. Fifth Edition. ACGIH, Cincinnati, Ohio.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was used. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to. However, external peer reviews on the Massachusetts methodology and guideline documentation have been carried out and public input was solicited at a minimum of two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE staff). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each individual AAL will undergo review at least every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

Massachusetts uses occupational literature as a database for assessing acute and chronic toxicity of chemicals, and to select a beginning number for use in deriving preliminary human exposure limits for chemicals with threshold effects. The Most Appropriate Occupational Limit (MAOL) is defined as the occupational limit which provides the best protection against the greatest number of documented health effects. The results of the scoring for acute and chronic health effects are obtained by combining the MAOL with a severity factor according to a scoring matrix. The weight-of-evidence classification for propylene oxide, for acute and toxic effects as well as animal and human carcinogenicity, places it in Group 'C' (limited animal evidence and no or inadequate human evidence). Using the EPA's Gene-Tox database as the source of scientifically valid data, propylene oxide was given a score of 'D' for limited evidence of mutagenicity on the basis of positive results on primary short-term tests (cell transformation

studies, hamster embryo cells), in forward reverse mutation (*N. crassa*, *S. cerevisiae*), in a sex-linked recessive lethal test (*Drosophila*).

The Allowable Ambient Limit (AAL) for propylene oxide corresponding to an excess lifetime cancer risk of 3.6×10^{-6} was determined to be $0.3 \mu\text{g}/\text{m}^3$. AALs are based on both threshold and non threshold health effects and correspond to either the Threshold Effects Exposure Limit (TEL) or the Non-threshold Effects Exposure Limit (NTEL) whichever is lower. In this case, the NTEL of $0.3 \mu\text{g}/\text{m}^3$ is lower than the TEL of $6 \mu\text{g}/\text{m}^3$, the AAL is $0.3 \mu\text{g}/\text{m}^3$. The State of Massachusetts has adopted the US EPA's cancer risk assessment in deriving the non-threshold effects exposure limit. No basis for the TEL was provided, but it is equivalent to the US EPA RfC divided by 5 to account for multimedia exposure.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical is set at 1×10^{-6} . The Division of Air Quality Control plans to employ the AALs in the permitting, compliance, and enforcement components of the air toxics program.

10. Multimedia Considerations of Guidelines:

In deriving the TEL guideline, a multimedia exposure adjustment factor of 20% is systematically applied as a relative source contribution factor. On the other hand, the AAL does not consider other sources of exposure. When adequate cancer potency data exist, the State of Massachusetts develop non-threshold effect exposure limit (NTEL) by applying a non-threshold effects uncertainty factor (NTEUF). The AAL will then continue to be the lower of the values of the TEL or the NTEL (ORS, 1994).

11. Other Relevant Factors:

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Propylene oxide

2. *Agency:* Michigan (Department of Natural Resources)

3. *Guideline Value(s):*

The Initial threshold screening levels (ITSL) is $30 \mu\text{g}/\text{m}^3$ (24-hour average) for propylene oxide based on the US EPA reference concentration (RfC) of $30 \mu\text{g}/\text{m}^3$ (US EPA, 1990). For protection against carcinogenicity risk, Michigan has established an initial risk screening level (IRSL) and a secondary risk level (SRSL) using the unit risk calculated by the US EPA (3.7×10^{-6} per $\mu\text{g}/\text{m}^3$). The initial risk screening level is $0.3 \mu\text{g}/\text{m}^3$ (annual average) corresponding to a cancer risk level of 10^{-6} . The secondary risk screening level is $3 \mu\text{g}/\text{m}^3$ corresponding to a risk level of 10^{-5} .

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxics rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. Furthermore, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level for new or modified emission process.

5. *Documentation Available:*

Michigan Department of Natural Resources/Environmental Quality, 1995/1997. Air Toxics Screening Levels. Air Quality Division.

Key Reference(s):

US EPA, 1996. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months while a complete list of all screening levels is published at the beginning of each year.

8. *Key Risk Assessment Considerations:*

When IRSL and SRSL values are established for carcinogens, they are based on the cancer potency values published by the US EPA in the IRIS database. If these values are not available then the EPAs HEAST values are used as the basis. If none of these are found then the toxicologist establishes the

screening levels using inhalation toxicity data, if available. Michigan uses the same data as the US EPA for the determination of unit risk.

For propylene oxide, Michigan has adopted the US EPA's RfC of $30 \mu\text{g}/\text{m}^3$ and its inhalation cancer unit risk of 3.7×10^{-6} per $\mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

No Information.

11. Other Relevant Factors:

No Information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Propylene oxide

2. *Agency:* New Jersey

3. *Guideline Value(s):*

New Jersey has adopted the US EPA's reference concentration of $30 \mu\text{g}/\text{m}^3$ and the cancer unit risk of 3.7×10^{-6} per $\mu\text{g}/\text{m}^3$.

4. *Application:*

The list of reference concentrations for inhalation are maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consist of two levels. The first level risk screening uses information from permit applications and generalised worst case assumptions to estimate non-cancer and cancer risk from inhalation. Sources which fail the first level screening are submitted to a second level risk screening which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources which fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.).

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The risk screening procedure considers only inhalation exposure. Every source is not modelled individually. Instead, nomographs, developed using dispersion models, are used to calculate ambient air

concentrations of each source chemical. In the case of carcinogens, the averaging time is annual assuming ambient exposure levels to the chemical all the time. Long-term effects are calculated on the basis of the maximum annual average air concentration. In the case of carcinogens, this latter concentration is multiplied by the unit risk factor to obtain the incremental risk for a chemical. In addition, New Jersey believes that just because a chemical has not shown carcinogenicity, it is not a proven non-carcinogen.

In the case of propylene oxide, New Jersey has adopted both the reference concentration of $30 \mu\text{g}/\text{m}^3$ and the cancer unit risk of 3.7×10^{-6} per $\mu\text{g}/\text{m}^3$ developed by US EPA.

9. Key Risk Management Considerations:

Public health risk estimates of incremental risk for inhalation of carcinogens are calculated as a product of the maximum annual average ambient air concentration of a chemical ($\mu\text{g}/\text{m}^3$) and the chemical-specific unit risk factor ($\mu\text{g}/\text{m}^3$)⁻¹. The AQPP uses this information for its risk management. The policy has the following three guidelines: (1) if the incremental cancer risk is less than 1 in 10^{-6} , the risk is considered negligible, (2) if the risk is greater than 1 in 10^{-4} , the risk is considered unacceptable, and (3) if the risk lies between the preceding two values, the risk is evaluated on a case-by-case basis.

10. Multimedia Considerations of Guidelines:

The risk screening procedure considers only exposure by the inhalation route.

11. Other Relevant Factors:

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Propylene oxide

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The current Short-term Guideline Concentration (SGC; 1-hour average air concentration) is 11,000 $\mu\text{g}/\text{m}^3$ and the Annual-average-based Guideline Concentration (AGC) is 110 $\mu\text{g}/\text{m}^3$. Propylene oxide is classified as a moderate toxicity air contaminant and is given an "B" 6NYCRR Part 212 Environmental Rating. The Department of Environmental Conservation plans to set new guidelines for propylene oxide in the next revision. Unofficially, the new values could be 0.3 $\mu\text{g}/\text{m}^3$ (AGC) and the SGC would remain unchanged (DeSantis, 1997).

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

Key Reference(s):

DeSantis, S., 1997. Personal communication. New York Department of Environmental Conservation (DEC).

American Conference of Governmental Industrial Hygienists, 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Ohio, Cincinnati.

United States Environmental Protection Agency (US EPA). 1986. Guidelines for Carcinogen Risk Assessment. Federal Register 51: 33992-34003. (9/24/86).

6. Peer Review Process and Public Consultation:

The scientific documents prepared by the New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guidelines development process.

7. Status of Guideline:

Current. The New York State Air Guide - 1 is dated 1991. The latest version of the companion Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

8. Key Risk Assessment Considerations:

Propylene oxide is classified as a moderate toxicity air contaminant by New York State (1994). This classification includes animal oncogens, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans. It includes those chemicals for which oncogenicity has been demonstrated in at least one mammalian species, but do not meet the carcinogenicity criteria for HIGH toxicity classification. It also include those chemicals which have been shown to damage DNA or chromosomes in *in vitro* and/or *in vivo* short-term tests and those chemicals that are known to cause adverse reproductive and developmental effects in at least one mammalian species which do not meet the criteria for HIGH toxicity classification.

Both the current Short-term Guideline Concentration and the Annual Guideline Concentration were derived from the occupational threshold limit values (time-weighted average) developed by the American Conference of Government Industrial Hygienists (ACGIH).

9. Key Risk Management Considerations:

Environmental Ratings are reviewed for each contaminant every time a Certificate to Operate comes up for renewal. A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses to be employed in the permitting process.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

No information.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Propylene oxide

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

No guideline.

4. *Application:*

The WHO Air Quality Guidelines are intended to provide a basis to protect public health from adverse effects of air pollution, and to provide background information and guidance to governments in making risk management decisions. However, it should be noted that no standards as such are promulgated by the WHO.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark, 426 p.

Key Reference(s):

None

6. *Peer Review Process and Public Consultation:*

Scientific background documents were prepared by experts and submitted to working groups consisting of international experts to provide a basis for discussion. After a series of meetings and internal and external reviews by experts and representatives of the Member States of the Region, the resultant conclusions and recommendations were presented at a final meeting where they were adopted by consensus of the representatives. In addition, peer-reviewed scientific research data were employed in the development of these documents.

7. *Status of Guideline:*

Currently not applicable.

8. *Key Risk Assessment Considerations:*

None.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

None

11. *Other Relevant Factors:*

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Propylene oxide

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

A national air limit value does not exist for propylene oxide. Propylene oxide is attributed a C.3 code, which means that it is considered a human carcinogen with no threshold value. This category is assigned an immission concentration equal or greater than $0.1 \mu\text{g}/\text{m}^3$ at which risk of one extra cancer case per 1 million people given a lifelong exposure arises. As a result, the Netherlands has set the target value for propylene oxide at $1 \mu\text{g}/\text{m}^3$ based on cancer risk from lifetime exposure. Propylene oxide is listed as belonging to IARC (International Agency for Research on Cancer) code 2A (probably carcinogenic to humans) and to European Community (EEC) code 2C (carcinogenic to humans due to evidence obtained by mainly chronic animal tests).

4. *Application:*

Limit values are non-statutory environmental quality objectives that are considered policy guidelines. They should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effect-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effect-oriented guidelines.

The Netherlands utilizes a progressive criteria setting process in implementing the effects-oriented policy. The objective is to reduce the emission of priority substances gradually to below a target value concentration. The policy defines a maximum permissible concentration based on toxicological evaluation and a negligible concentration which is set at 1/100 of the maximum permissible concentration. The negligible concentration is meant to be indicative of an environmental quality at which the risks of adverse effects are considered negligible. These risks apply to ecosystems, functional properties of the environment and other compartments. The target value is set to the negligible concentration or the naturally occurring background level. If the target value can only be met in a long-term, intermediate objectives (limit or guidance values) will be used. In the course of time, the limit or guidance values will be tightened to reach the target value.

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 pp. + Appendices.

Van de Plassche, E.J., and G.J.M. Bockting, 1993. Towards Integrated Environmental Quality Objectives for Several Volatile compounds. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Report no. 679101 011.

Key Reference(s):

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances, but are only available in Dutch.

6. Peer Review Process and Public Consultation:

No specific information on this issue was presented in the available English documentation.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

Propylene oxide is considered to be a carcinogen, class C.3, under the Netherlands Emission Regulations. This category is assigned an immission concentration equal or greater than $0.1 \mu\text{g}/\text{m}^3$ at which risk of one extra cancer case per 1 million people given a lifelong exposure arises.

9. Key Risk Management Considerations:

Risk management is carried out by progressive criteria setting. In principle the target value is set to the negligible concentration or the naturally occurring background value, whichever is higher. A limit value should not be exceeded and a guidance value should be avoided whenever possible. With time, the values are tightened to reach the target value.

Carcinogens without a threshold value are subject to compulsory minimisation under Netherlands Emission Regulations. Propylene oxide is black-listed for emission into air in the Netherlands. Substances are placed on this list on the basis of their environmentally harmful properties and not on the risk estimate of the substance. Furthermore, the black list is only relevant to source-oriented policy. The best available means (bam) has to be used to reduce pollution by this substance. Since these substances may occur naturally or may be produced from other countries, the substance(s) may be included on a priority substance list for special attention.

10. Multimedia Considerations of Guidelines:

Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. Information is currently available on the MPC and the NC (negligible concentration) of water, soil, sediment and air.

11. *Other Relevant Factors:*

No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Propylene oxide

2. *Agency:* Swedish Environmental Protection Agency

3. *Guideline Value(s):*
No guidelines.

4. *Application:*
No information.

5. *Documentation Available:*
Victorin, K., 1993. Health effects of urban air pollutants: guideline values and conditions in Sweden. *Chemosphere* 27: 1691-1706.

Victorin, K., 1997. Personal communication.

Key Reference(s):
None.

6. *Peer Review Process and Public Consultation:*
No information.

7. *Status of Guideline:*
No information.

8. *Key Risk Assessment Considerations:*
No information.

9. *Key Risk Management Considerations:*
No information.

10. *Multimedia Considerations of Guidelines:*
No information.

11. *Other Relevant Factors:*
No information.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Propylene oxide

2. *Agency:* Environment Canada

3. *Guideline Value(s):*

No information.

4. *Application:*

No information.

5. *Documentation Available:*

Canadian Environmental Protection Act (CEPA), 1993-94. CEPA Priority Substance List (PSL-1)-
Assessment Reports (Environment and Health Canada).

Key Reference(s):

This compound was not considered under PSL-1 and will not be considered under PSL-2.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
TOLUENE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Toluene was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing standard in 1970. A review of scientific and technical information relevant to setting an ambient air quality standard for toluene has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for toluene.

Toluene is a colourless, volatile liquid with a benzene-like odour. Odour detection thresholds for toluene range from 0.6 to 140 mg/m³, with a geometric mean of 6 mg/m³.

Toluene is predominantly used in the production of benzene. It is also used as an octane enhancer in gasoline, and as a raw material in the manufacture of toluene diisocyanate. In addition, it is used as a solvent in aerosol spray paints, wall paints, lacquers, inks, adhesives, gums, resins, and in such consumer products as spot removers, paint strippers, cosmetics, perfumes, and antifreeze.

According to the information from the National Pollutant Release Inventory (NPRI), between reporting years of 1993 and 1997, approximately 150 industrial sources reported toluene air releases in Ontario totalling 4,245 to 5,630 tonnes. Releases to air represent greater than 99 % of the total releases to all media in Ontario. Data indicate that in these five reporting years, toluene was among the top substances of release quantities in Ontario as well as in Canada.

Toluene is easily absorbed via the lungs and gastrointestinal tract in both humans and animals. Inhalation is likely the primary pathway of toluene exposure. Once absorbed, toluene tends to accumulate in adipose tissue, in tissues with high fat content, and in highly vascularized tissues, such as nerve cells and brain tissues.

Toluene adversely affects the central nervous system of humans and experimental animals. The severity of the effects is related to increases in toluene levels, however, data from occupational and epidemiologic studies do not appear to support a duration-response relationship in toluene-induced neurotoxicity. Symptoms observed in exposed humans range from a decrease in psychometric performances (particularly related to visual perception), to headaches, intoxication, convulsions, narcosis, and death. Euphoria, dilated pupils, convulsions, nausea, and dizziness have also been reported. Toluene also causes irritation to the eyes and to the upper respiratory system. Prolonged or repeated exposure increases the severity of damage to the upper respiratory system and can induce

toxic effects to the liver and kidney. Exposure to high levels of toluene can result in adverse effects to developing fetuses of both humans and animals.

Toluene does not appear to be genotoxic. This chemical is not classified as a human carcinogen by the United States Environmental Protection Agency and International Agency for Research on Cancer due to insufficient animal data and the absence of human data. Health Canada concluded that toluene was unlikely to be carcinogenic to humans based on similar considerations.

Ontario currently has a 24-hour AAQC and a half-hour POI standard of $2,000 \mu\text{g}/\text{m}^3$ for toluene. These criteria have been established on the basis of the odour effect of toluene.

In revising the air quality standards for Ontario, the Ministry of the Environment is reviewing risk assessments and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. The US EPA has developed an inhalation Reference Concentration (RfC) of $400 \mu\text{g}/\text{m}^3$. The World Health Organization has recommended a guideline value of $7500 \mu\text{g}/\text{m}^3$. The Canadian federal agencies of Health and Environment have established a Tolerable Concentration of $3750 \mu\text{g}/\text{m}^3$. All these criteria were derived for the protection of the central nervous system from the effects of toluene. A majority of the U.S. state agencies studied adopted the RfC of the US EPA. In addition, the World Health Organization recommended an odour-based guideline of $1000 \mu\text{g}/\text{m}^3$.

Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the RfC of the US EPA, the Tolerable Concentration of Health Canada and the Air Quality Guideline of the World Health Organization. Of these, the Tolerable Concentration of $3,750 \mu\text{g}/\text{m}^3$ developed by Health Canada is considered the most appropriate basis for air quality standards development for Ontario. Deriving a 24-hour AAQC from the Tolerable Concentration will result in a criterion higher than the current Ontario odour-based 24-hour AAQC. Therefore, replacing the odour-based POI and 24-hour AAQC of $2,000 \mu\text{g}/\text{m}^3$ is not recommended.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information and odour property, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for toluene:

- a 24-hour average AAQC of 2,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for toluene based on the odour nuisance and the adverse health effects of this compound; and,
- a half-hour average POI of 2,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for toluene based on the odour nuisance of this compound.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Toluene was identified as a priority for review based on both, its pattern of use in Ontario and recent toxicological information that has been published subsequent to the development of the existing standard in 1970. A review of scientific and technical information relevant to setting an ambient air quality standard for toluene has previously been provided to stakeholders for their comments. This document therefore provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour point of impingement (POI) standard for toluene.

2.0 General Information

2.1 Physical/chemical Properties

The following list provides some general information on toluene and its properties:

CAS #	108-88-3
RTECS #	XS5250000
UN #	1294
Conversion Factors	1 ppm = 3.77 mg/m ³ @ 25 °C and 1 atm. 1 mg/m ³ = 0.27 ppm @ 25 °C and 1 atm.
Boiling Point	110.6 °C
Flash Point	4.40 °C
Henry's Law Constant	6.61 x 10 ⁻³ atm m ³ /mol @ 25 °C
Log K _{ow}	2.69 @ 25 °C
Formula	C ₇ H ₈
Molecular Weight	92.13 g/mol
Vapour Density (air = 1)	3.14
Vapour Pressure	22 mm @ 20 °C
Common Synonyms	Methylbenzene, toluol, and phenylmethane

Toluene is a colourless, volatile liquid with a benzene-like odour (Lewis, 1992). According to the report of the American Industrial Hygiene Association (AIHA), the acceptable odour detection thresholds range from 0.6 - 140 mg/m³ (0.16 - 37 ppm), with the geometric mean at 6 mg/m³ (1.6 ppm), and the recognition odour thresholds range from 7.2 - 260 mg/m³ (1.9 - 69 ppm) (AIHA, 1989). The odour threshold for 50% detection is reported to be 12 mg/m³ (Nagi, 1991)

2.2 Uses of Toluene

Toluene is predominantly used in the production of benzene (Environment Canada, 1993). It is also used as an octane enhancer in gasoline, and as a raw material in the manufacture of toluene diisocyanate. In addition, it is used as a solvent in aerosol spray paints, wall paints, lacquers, inks, adhesives, natural gums, resins, and in such consumer products as spot removers, paint strippers, cosmetics, perfumes, and antifreezes (US EPA, 1994).

2.3 Sources and levels

Sources

Toluene is a natural component of coal and petroleum (Kirk *et al.* 1983). As such, all toluene present in gasoline in Canada is derived from the normal refining process of petroleum (Environment Canada, 1992). The most common refining process is the dehydrogenation of naphtha feedstock (Environment Canada, 1984). Evaporation of gasoline, which is 5-7% toluene, and car exhaust are the largest sources of toluene emissions to air in the United States (US EPA, 1994). Toluene is also a by-product of cigarette smoking (WHO, 1985)

Toluene is listed in Environment Canada's National Pollutant Release Inventory (NPRI), for the report of emissions by the facilities in Canada (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996; NPRI, 1997). Toluene had been among the top pollutants in terms of release quantities between reporting years of 1993 - 1997. The atmospheric releases in Canada for the reporting years of 1993, 1994, 1995, 1996 and 1997 for 300 facilities, were 7271, 7659, 6761, 6007 and 6904 tonnes, respectively. Information from these reporting years indicates that the emissions were relatively consistent. Atmospheric releases in Ontario followed a similar pattern. The releases for 1993, 1994, 1995, 1996 and 1997 were 5467, 5631, 4829, 4245 and 4517 tonnes, respectively. About 65 to 75% of the national emissions came from approximately 125 to 170 facilities in Ontario. Atmospheric emissions accounted for over 99% of the total toluene releases from all media in Ontario. The major industrial sources of atmospheric toluene emissions in Ontario include, the transportation equipment industries, paper products industries, plastic products industries, and the printing and publishing industries. Other important sources include industries that produce refined petroleum and coal products, chemical and chemical products, as well as leather products.

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 248 Certificates, covering emissions of toluene to the atmosphere, was identified. The majority of these approvals were issued to paint spray operations, consistent with the widespread use of toluene as a solvent in paint. A significant number of Certificates of Approval were also issued for exhaust from vents, fumehoods and other exhaust systems for a variety of other chemical processes, such as chemical and chemical product industries. The median Ground Level Concentration (GLC) predicted by Regulation 346 dispersion modelling, for all 248 sources, was approximately $60 \mu\text{g}/\text{m}^3$. The maximum and minimum GLCs predicted were 1,886 and $0.0002 \mu\text{g}/\text{m}^3$, respectively. The median GLC predicted for the paint spray sources was the highest, at $103 \mu\text{g}/\text{m}^3$, as compared to the predicted GLC values for other operations including, $23 \mu\text{g}/\text{m}^3$ for exhaust, and $16 \mu\text{g}/\text{m}^3$ for chemical and chemical products industries.

Due to releases from several indoor sources, toluene concentrations in indoor air are often greater than outdoor ambient air concentrations. Indoor sources include toluene-based products such as paints, adhesives, coatings, finishes, paint removers, paint thinners, upholstery and carpet cleaners, protectors, and contact cement (Environment Canada, 1993). Cigarette smoke also emits toluene, at a rate of 80 $\mu\text{g}/\text{cigarette}$, to the air (US EPA, 1994).

Ambient Air Concentrations

Ambient air monitoring data from Environment Canada and Ontario Ministry of the Environment indicated that the annual average level of toluene in the rural areas ranged from 0.36 to 3.85 $\mu\text{g}/\text{m}^3$ (24-hour averaging time) between 1990 and 1995, with the highest concentration in Longwoods at 27.9 $\mu\text{g}/\text{m}^3$ in 1994 (Steer, 1997). The levels are generally higher in urban centres, with annual average concentrations ranging from about 1.31 to 15.19 $\mu\text{g}/\text{m}^3$ within the same time period (1990-1995), possibly as a result of motor vehicle emissions (Steer, 1997).

Higher concentrations could be observed in the vicinity of industrial sources. For example, the toluene level (24-hour averaging time) in outdoor air at an industrial complex at Elmira was reported to range from 0.53 to 94 $\mu\text{g}/\text{m}^3$, between April 1993 and May, 1996. The mean value over this time period was 18.46 $\mu\text{g}/\text{m}^3$ (Steer, 1998). Half hour measurements of toluene in the air have been taken on occasions in the surroundings of some major emitting facilities including petroleum refinery plants. The average concentrations at downwind locations ranged from 9.4 $\mu\text{g}/\text{m}^3$ to 21 $\mu\text{g}/\text{m}^3$, as compared to 1.04 - 4.7 $\mu\text{g}/\text{m}^3$ at upwind locations (MOE, 1998b).

The highest ambient concentrations of toluene were recorded in the immediate vicinity of gas stations as a result of volatilization from gasoline. The overall average concentrations at Canadian gas stations were 535 $\mu\text{g}/\text{m}^3$ (0 to 6,450 $\mu\text{g}/\text{m}^3$) in the winter and 202 $\mu\text{g}/\text{m}^3$ (0 to 14,500 $\mu\text{g}/\text{m}^3$) in the summer. Mean toluene concentrations taken near the pump were 1,880 $\mu\text{g}/\text{m}^3$ (70 to 10,000 $\mu\text{g}/\text{m}^3$) in the winter and 2,550 $\mu\text{g}/\text{m}^3$ (20 to 20,200 $\mu\text{g}/\text{m}^3$) in the summer (Environment Canada, 1992). These facilities would be considered point sources of toluene exposure.

Toluene concentrations have also been measured in samples of indoor air. Indoor air samples were taken from 18 homes near an abandoned waste disposal site in Montréal. The mean toluene concentration was 37 $\mu\text{g}/\text{m}^3$ (detection limit of 0.1 $\mu\text{g}/\text{m}^3$), which was not significantly different from concentrations in control homes located elsewhere (Environment Canada, 1992). Indoor air samples were collected from twelve homes in the Toronto area in November or December 1986 (mean of 53.6 $\mu\text{g}/\text{m}^3$), and again in six of these homes in February or March 1987 (mean of 39.9 $\mu\text{g}/\text{m}^3$). Sources of toluene were not provided in this study (Environment Canada, 1992).

2.4 Environmental Fate

Most of the toluene released to the environment is emitted to the air. Toluene is a volatile organic compound (VOC) with an estimated half-life in the atmosphere of approximately 13 hours. Toluene is a member of a class of volatile organic chemicals (VOCs) that react with oxides of nitrogen in the presence of sunlight to form ground-level ozone, a component of smog. (US EPA, 1994). Toluene that is present in the water and the soil will evaporate readily into the atmosphere (US EPA, 1994). The primary degradation pathway for toluene in the atmosphere is photochemical breakdown, resulting in the production of hydroxyl radicals. Minor degradation pathways of toluene include oxidation reactions with nitrogen dioxide, oxygen, and ozone as well as photolysis (US EPA, 1994).

3.0 Toxicology of Toluene

The following toxicological review of toluene focusses primarily on inhalation. Inhalation is considered the predominant pathway of human exposure to toluene, illustrated by data from the NPRI which indicates that over 98% of the toluene released in Ontario is emitted into air. Data on other exposure media are included where relevant or where inhalation data is lacking.

Toluene is easily absorbed via the lungs and gastrointestinal tract, both in humans and animals. Absorption of inhaled toluene vapour is potentially of greater concern than dermal absorption of liquid toluene because liquid toluene rapidly evaporates (US EPA, 1994). Toluene tends to accumulate in adipose tissue, tissues with high fat content, and in highly vascularized tissues, such as nerve cells and brain matter (US EPA, 1994). Toluene is readily metabolized and mainly excreted from the body in urine in the form of its conjugated metabolites. The rest (10-20%) is excreted as unchanged toluene through the lungs. Excretion is generally complete within 24 hours after exposure (US EPA, 1994).

In general, the adverse effects of toluene are similar in humans and animals (Calabrese and Kenyon, 1991; US EPA, 1994).

3.1 Acute Toxicity

Humans exposed to intermediate to high levels of toluene for short periods exhibit adverse central nervous system (CNS) effects, ranging from headaches, to dizziness and intoxication, convulsions, narcosis, and death. Other symptoms include mild throat and eye irritation, along with euphoria, dilated pupils, convulsions, and nausea (US EPA, 1994). The severity of the effect increases with the level of exposure. Effects on the CNS such as headaches, dizziness and intoxication, and eye irritation were observed in humans exposed to toluene at 100 ppm (377 mg/m³) for 6 hours/day for 4 days. Exposure to 600 ppm (2260 mg/m³) resulted in more serious symptoms such as euphoria, dilated pupils,

convulsions and nausea. Narcosis and death have been reported at 10000 - 30000 ppm (37000 - 113100 mg/m³).

In an inhalation study with human volunteers, sixteen young, healthy males were exposed to toluene ranging from 10 to 100 ppm (37.7 to 377 mg/m³) for 6 hours (Anderson *et al.*, 1983 as cited in OEHHA, 1998). At 377 mg/m³, headache, dizziness, a feeling of intoxication, and slight eye and upper respiratory irritations were reported. The subjects also complained that it became more difficult to participate in the battery of psychometric tests and that their reaction time felt impaired at this exposure level. No significant objective changes were observed in the performance tests when compare with those of the controls. No symptoms were reported at the 37.7 mg/m³ and 151 mg/m³ (40 ppm) exposure levels.

The LC₅₀ (lethal concentration, 50% killed) reported are 5320 ppm (20056 mg/m³) for mice for 7 hours, and 4618 ppm (17410 mg/m³) for rats for 6 hours. The initial effects of toluene exposure are instability and incoordination, lacrimation and sniffles, followed by narcosis. Animals die of respiratory failure from severe nervous system depression. Cloudy swelling of the kidneys was observed in rats exposed to 1600 ppm (6032 mg/m³) for 18 - 20 hours per day for 3 days (US EPA, 1994).

3.2 Subchronic/Chronic Toxicity

Long-term exposure to toluene results in adverse effects on the CNS and induces respiratory irritation in both humans and animals. In addition to CNS effects, repeat doses of toluene or very high exposure concentrations cause liver and kidney damage (Calabrese and Kenyon, 1991; US EPA, 1994). Similar effects have been observed in animals on a chronic exposure (US EPA, 1994).

3.3 Developmental/Reproductive Toxicity

Exposure to high levels of toluene can result in adverse effects in a developing fetus for both humans and animals. Adverse effects were seen in three children whose mothers had abused toluene during their pregnancies. All three children suffered from microcephaly, CNS dysfunction, attention deficits, and delayed development or mental deficiency. Other common physical effects include a small midface and jaw, deep-set eyes, and blunted fingertips (US EPA, 1994).

Delayed skeletal development was reported in mice at toluene levels which were not apparently maternally toxic (Calabrese and Kenyon, 1991). This effect was also observed in fetuses of rats exposed to 1,000 mg/m³ for 8 hours/day during gestational days 1-21. Treatment of CFLP mice to 500 or 1,500 mg/m³ toluene, continuously during days 6-13 of gestation, did not have fetuses with skeletal abnormalities, and all dams died at the high dose during the first 24 hours of exposure (US EPA, 1994).

3.4 Genotoxicity

Gene mutation tests using bacteria, yeast, and fruit flies yielded negative results (US EPA, 1994). Negative results have also been reported in human cells using *in vitro* sister chromatid exchange assays and in male mice using sperm morphology assays (GENETOX, 1997; Calabrese and Kenyon, 1991; US EPA, 1994). However, other sister chromatid exchange and chromosome aberration mammalian (including human) *in vitro* assays (Calabrese and Kenyon, 1991; US EPA, 1994) yielded conflicting results. Responses of rodent micronucleus tests were positive when toluene was administered by injection, but negative via the oral route. Based on a weight of evidence assessed, it was suggested that toluene was not genotoxic in mammalian or microbial systems (Environment Canada, 1992).

3.5 Carcinogenicity

Epidemiological studies revealed no significant risk of cancer among workers who had been exposed to toluene for at least 5 years (US EPA, 1994).

The only 2-year chronic inhalation bioassay with rats of both sexes resulted in no carcinogenic response (CIIT, 1980). This study was considered inadequate (US EPA, 1997) because the highest dose administered was well below the maximum tolerable dose (MTD) for toluene, and because of the high incidence of pathological changes in the control animals. Considering inadequate human and animal carcinogenicity data, both the United States Environmental Protection Agency (US EPA, 1997) and the International Agency for Research on Cancer (IARC, 1989) did not consider toluene a human carcinogen. Based on the same set of evidence, Health Canada (1996) concluded that toluene was unlikely to be carcinogenic to humans (Group IV). The conclusions of these three agencies do not support regulating toluene as a human carcinogen.

3.6 Environmental Effects

Toluene is very toxic to early life stages of leopard frog (*Rana pipiens*) and northeastern salamander (*Ambystoma gracile*). Toluene exposure from 30 minutes after egg fertilization to 4 days post hatch resulted in a 9-day LC_{50} value of 0.39 mg/L for the frog and a 9.5-day LC_{50} of 0.85 mg/L for the salamander (CEPA, 1992). Exposure of earthworms (*Eisenia foetida*) to toluene in soil resulted in a no-observed-effect-concentration (NOEC) of 34 mg/kg, a lowest-observed-effect-level (LOEC) of 71 mg/kg and an LC_{50} of 126 mg/kg (Environment Canada, 1996).

In plants, toluene caused signs of toxic effects, including chlorosis and growth inhibition at concentrations of $> 6,000 \text{ mg/m}^3$ in air, however, enhanced growth was observed at 5 to $50 \mu\text{g}$ toluene/L of aqueous medium (UK Department of the Environment, 1991).

Acute exposures of toluene are moderately toxic to aquatic organisms. Ninety-six-hour LC_{50} values for toluene exposure in fish range from 5.5 mg/L for Coho salmon fry (*Oncorhynchus kisutch*) (Moles et al, 1981) to 1,180 mg/L for mosquito fish (*Gambusia affinis*) (US EPA, 1980). Studies of chronic exposures of toluene to fish resulted in 28-day no-observed-adverse-effect concentration (NOAEC) ranging from 3.2 mg/L and 7.7 mg/L for Sheepshead minnow and a 40-day NOAEC ranging from 1.4 mg/L to 2.8 mg/L for Coho salmon (WHO, 1985).

Photosynthesis inhibition of marine plankton occurred at toluene concentrations of 34 mg/L (Potera, 1975). Toluene is not toxic to microorganisms at concentrations of 100 mg/kg soil (Anderson et al, 1991), however microbial activity was temporarily (6 days) depressed at toluene concentrations of 1,000 mg/kg soil (Walton et al, 1989).

4.0 Existing Air Quality Regulations

4.1 Overview

Ontario currently has a half-hour POI standard and a 24-hour AAQC, both are set at $2,000 \mu\text{g}/\text{m}^3$. These criteria were established on the basis of odour effects in 1970 (MOEE, 1994a). According to the potential health effects of toluene, such as the neurological, respiratory irritation and developmental effects of toluene, these criteria are considered out of date and require reviewing.

The documentation for ten agencies, including the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government, was reviewed for the existence and the basis of their air quality criteria for toluene. A brief summary of this review is presented in Table 1, and agency-specific summaries of information concerning air quality guidelines for toluene are presented in Section 11.0, the Appendices of this report.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria, based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria, based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

One common observation is that the scientific rationales supporting the various agency's ambient air quality criteria are based on the protection of humans from the neurological and respiratory irritation effects of toluene. Most of the state agencies in the United States establish their air guidelines based on the inhalation Reference Concentration (RfC) of $400 \mu\text{g}/\text{m}^3$ developed by the US EPA (US EPA, 1992 & 1997). This RfC is derived from the data in an occupational study for the CNS effects of toluene. The state of Michigan adopted the RfC of the US EPA for its air guideline of $400 \mu\text{g}/\text{m}^3$ (State of Michigan, 1997). The Commonwealth of Massachusetts derived their exposure limits, the Threshold Effects Exposure Limits (TEL; $80 \mu\text{g}/\text{m}^3$) and Non-threshold Effects Exposure Limits (NTEL; $20 \mu\text{g}/\text{m}^3$), based on the RfC (MDEP, 1995).

New York State adopted the RfC as its annual guideline concentration (AGC) of $400 \mu\text{g}/\text{m}^3$, but derived its short-term guideline based on the occupational exposure limit (threshold limit value-time weighted average, TLV-TWA) of $188 \text{ mg}/\text{m}^3$ (50 ppm), developed by American Conference of Governmental Industrial Hygienists (ACGIH) (NYSDEC, 1991). The ACGIH recommended this TLV-TWA for the prevention of headaches, irritation, and reduction in cognitive response among workers exposed occupationally to toluene (ACGIH, 1991).

The California Environmental Protection Agency (California EPA) (California EPA, 1997a) adopted the Applied Action Level (AAL) of $200 \mu\text{g}/\text{m}^3$, developed by their Department of Toxic Substances Control (DTSC), as their risk-based chronic reference exposure level (REL). The AAL was based on a study of the developmental and reproductive toxicity of toluene in CD-1 mice by gavage (Nawrott and Staples, 1977). The AALs developed by the DTSC are no longer applied, therefore the REL for toluene is out of date. The California EPA is in the process of developing a revised chronic inhalation REL of $400 \mu\text{g}/\text{m}^3$, based on the RfC of the US EPA (OEHHA, 1997). Furthermore, the California EPA is also proposing an acute REL of $37,000 \mu\text{g}/\text{m}^3$, based on the central nervous system effects, eye, nose and respiratory irritation, and reproductive and developmental effects (OEHHA, 1998).

Table 1. Summary of Existing Air Quality Guidelines¹ for Toluene

Agency	Guideline Value	Basis of Guideline	Date ¹	Comments
US EPA (IRIS)	400 µg/m ³	Study of CNS effects in humans exposed occupationally	1992	Non-cancer endpoint; RfC (Reference Concentration):
California	200 µg/m ³ proposed chronic REL: 400 µg/m ³ proposed acute REL: 37000 µg/m ³	AAL from California's DTSC. Neurological disturbances nervous system; nose, eye and respiratory irritation; reproductive/developmental effects	1993	Reference Exposure Level (REL): REL is currently being revised.
Massachusetts	80 µg/m ³ (24-hour average) 20 µg/m ³ (annual average)	RfC from US EPA. RfC from US EPA	1995 1995	Threshold Effects Exposure Limit (TEL); adjusted to allow for exposures via other media. Allowable Ambient Limit (AAL); adjusted for non-threshold effects
Michigan	400 µg/m ³ (24-hour average)	RfC from US EPA.	1997	Initial Threshold Screening Level (ITSL); Permitting standard, i.e., Predicted Ambient Impact of a toxic from any facility cannot exceed its ITSL
New Jersey	Reference Concentration (RfC): 400 µg/m ³ (annual average)	RfC from US EPA.	1994	Permitting application. RfC must be used in risk assessments conducted as part of a permit application.
New York State	45,000 µg/m ³ (1-hour average) 400 µg/m ³ (annual average)	TLV-TWA from ACGIH. RfC from US EPA.	1997 1997	Short-term Guideline Concentration (SGC); Used for permitting. Annual Guideline Concentration (AGC); Used for permitting.
WHO	7,500 µg/m ³ (24-hour average) ~1,000 µg/m ³ (30-minute average).	CNS effects in humans. Odour detection	1987	Air Guideline
Netherlands	100,000 µg/m ³ (½-hour average). 240 µg/m ³ (annual average):.	Emission standard. Province of Groningen's guideline.	1994	Used for permitting. National Maximum Immissible Concentration (MIC); Target value: to be identified.
Sweden	40.5-405 µg/m ³ (long-term average)	Health.	1993	Supporting documentation was only available in Swedish.
Canada (CEPA)	3,750 µg/m ³	Controlled experimental study of neurological and respiratory effects in humans.	1992	TC (Tolerable Concentration)
Ontario	2,000 µg/m ³ (24-hour average) 2,000 µg/m ³ (half-hour POI)	Both the POI and AAQC are based on odour.	1970	Ambient Air Quality Criterion Point of Impingement standard

- Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
- Date here refers to when the health-based guideline background report or the original legislative initiative was issued. The sources were the respective agency documents. For the US EPA, date refers to when the latest review of the RfC was conducted, if applicable, or the date the IRIS database was accessed, in the case where no RfC has been developed.

The World Health Organization (WHO), The Netherlands, Sweden and Health Canada have established their own exposure limits or guideline values. The WHO recommended a guideline value of $7,500 \mu\text{g}/\text{m}^3$ (daily average exposure) based on CNS effects in humans (WHO, 1987). An odour detection threshold of $1000 \mu\text{g}/\text{m}^3$ (30-minute average) was also suggested as appropriate as an air quality guideline. The Netherlands has set an emission standard for toluene which is used for permitting applications, and a National Maximum Immiscible Concentration (MIC) based on the Province of Groningen's guideline. Sweden has an air guideline set at $40.5 - 405 \mu\text{g}/\text{m}^3$ (long term average) for toluene, based on its effects on the central nervous system in humans. Environment Canada (1992), under the *Canadian Environmental Protection Act* (CEPA), has identified a Tolerable Concentration (TC) of $3,750 \mu\text{g}/\text{m}^3$ for the protection of humans against neurological effects such as central depression, headaches and dizziness) and respiratory irritation effects.

4.2 Evaluation of Existing Criteria

Several parameters are important in deriving an effect-based ambient air criterion protective of health. These parameters include, the nature of the adverse health effects due to toluene exposure, the approaches taken to evaluate the health risk resulting from toluene exposure, and the kind of assumptions made in the risk assessment. Odour and environmental effects are also important factors. These factors will be considered in setting an ambient air quality criterion for toluene for Ontario.

4.2.1 Discussion on Human Health

Toluene is not considered carcinogenic to humans. However, toluene can cause irritation and injury to the respiratory system. It induces adverse central nervous system effects and, at high concentrations, liver and kidney damage. Exposure to high levels of toluene may also result in adverse effects in a developing fetus. It also has an unpleasant smell. Therefore, an ambient air quality criterion must be sufficiently protective against all of these adverse and aesthetic effects.

Neurological and respiratory irritant effects of toluene are considered the most sensitive effects supporting the air quality criteria of most of the agencies reviewed. Most of the U.S. state agencies support the assessment of the US EPA, and have adopted or will adopt the RfC of this agency for their air quality criteria. The federal Government of Canada (Health Canada) and the WHO have assessed toluene individually and established their own criteria. The scientific basis for the derivation of the guidelines from The Netherlands and Sweden is not available, therefore these criteria are not given further consideration. It would appear reasonable to evaluate the rationales supporting the RfC of the US EPA, the Tolerable Concentration of Health Canada and the air guideline of the WHO as an appropriate reference for the development of an Ontario ambient air quality criterion.

4.2.2 US EPA Risk Assessment

The US EPA Reference Concentration (RfC) represents a daily inhalation exposure of the human population, below which a non-cancer adverse health effect is unlikely to occur. In deriving the RfC, the US EPA considered both the CNS and respiratory irritant effects. Since US EPA could not identify a NOAEL (No-observed-adverse-effect level) for either of these effects from the literature, the US EPA decided to consider the LOAEL, (Lowest-observed-adverse-effect level) for both effects. The occupational study of Foo *et al.* (1990) was used for the CNS effects and the National Toxicology Program (NTP, 1990) study was used for the respiratory irritant effects. The US EPA considered the CNS effects to be a more severe and more relevant endpoint, and therefore chose to base the RfC on the LOAEL for this effect.

The Foo *et al.* (1990) cross-sectional study involved 30 female workers in an electronic assembly plant where toluene was emitted. The exposed and control groups were matched for age, ethnicity and use of medications. None used alcohol and all were non-smokers. Exposed workers were exposed to toluene air levels of 332 mg/m³ (88 ppm, TWA) and control workers to 49 mg/m³ (13 ppm). Both levels were averages of individual personal samples. The exposed had worked in the plant for a longer period than the controls, average of 5.7 years versus 2.5 years respectively. The exposed group performed significantly poorer in the neurobehavioural tests administered as compared to the control group. The LOAEL was identified to be 332 mg/m³ (88 ppm). Adjustment for the TWA occupational exposure to continuous exposure resulted in a LOAEL (HEC) (Lowest-observed-adverse-effect level, human equivalent concentration) of 119 mg/m³. Applying an uncertainty factor (UF) of 300 resulted in a RfC of 400 µg/m³. This uncertainty factor accounts for intraspecies variability (UF = 10), for the use of a LOAEL (UF = 10) and for database deficiencies (UF = 3).

There were limitations to the Foo *et al.* (1990) study. For example, possible co-exposure to other solvents was not addressed in the study. Although there was a clear indication that the control workers performed better than the exposed workers in the neurobehavioural tests, a linear regression of test results versus personal exposure concentrations resulted in a poor concentration-response relationship for each test. The paucity of exposure information, together with the small size of the cohort, limits the interpretation of the study. However, the study results were supported by a clinical study (Echeuerria *et al.* 1989 as cited by US EPA, 1997), in which toluene concentrations were carefully controlled at levels bracketing 88 ppm (332 mg/m³). The US EPA explained that although the data of the study of Echeuerria *et al.* (1989) was generated from short-term exposures (3-7 hours over a period of 142 days), the results may be considered relevant to long-term exposures, as several studies indicated the absence of a duration-response relationship in toluene-induced symptomatology (US EPA, 1997).

4.2.3 WHO Risk Assessment

The World Health Organization (WHO) recommends an air guideline value for toluene based on the avoidance of adverse CNS effects and respiratory irritation in humans. The WHO identified a lowest-observed-effect level (LOEL) of 375 mg/m^3 , based on observations of CNS effects and mucosal irritation in a number of short-term exposure studies involving occupationally and experimentally exposed individuals (WHO, 1987). The WHO applied a safety factor of 50 which they determined to be adequate in view of the data on negative effects in humans, the lack of evidence of a chronic effect, and the minimally adverse nature of the observed effects at the LOEL (WHO, 1987). This resulted in a recommended guideline level of 7.5 mg/m^3 ($7,500 \text{ }\mu\text{g/m}^3$) for a 24-hour averaging time.

An odour detection threshold of 1 mg/m^3 ($1,000 \text{ }\mu\text{g/m}^3$) was also suggested as appropriate as an air quality guideline by WHO, for the avoidance of odour complaints. No uncertainty factor was applied in the derivation of the odour threshold and the averaging time was recommended to be 30 minutes.

4.2.4 Health Canada Risk Assessment

Health Canada has identified a Tolerable Concentration (TC) for toluene. The TC is the concentration to which a person can be exposed over a lifetime without any significant increased risk to their health (Health Canada, 1994). The TC is based on a controlled clinical epidemiological study which investigated the neurological and respiratory irritation effects of a 4-day toluene exposure (Andersen *et al.*, 1983). This study established a no-observed-effects-level (NOEL) of 150 mg/m^3 in humans. After adjusting from a 6-hour daily dosing schedule to a 24-hour continuous exposure scheme, and applying a factor of 10 to account for intraspecies variation, Environment Canada, (1992) arrived at a TC of 3.75 mg/m^3 ($3,750 \text{ }\mu\text{g/m}^3$). Although, 3 out of 16 subjects were smokers, data analysis did not account for smoking. In addition, there was no uncertainty factor included to account for any data deficiencies in the calculation of the TC.

4.2.5 Comparison of US EPA, WHO and Health Canada Risk Assessments

One common feature of the rationales supporting the ambient air quality criteria of the US EPA, the Canadian Federal Government, and the WHO, is that the effects of toluene on the central nervous system were considered and data from human studies were evaluated. However, the values of these criteria vary quite differently, from $400 \text{ }\mu\text{g/m}^3$ to $7500 \text{ }\mu\text{g/m}^3$. In light of these discrepancies, a more detailed examination of the scientific basis associated with these criteria, and the methods employed for their derivation by the three respective agencies, was performed. The results are outlined in Table 2.

Toluene-induced neurotoxicity has been documented in humans over a broad spectrum of severity that correlates with concentration (US EPA, 1997; WHO, 1987). The data obtained from studies of

occupationally exposed groups are fairly consistent with those from controlled human exposure experiments (WHO, 1987). In fact, the lowest effect levels (332-375 mg/m³) identified by US EPA (from occupational studies), WHO (from a combination of occupational and human volunteers studies), and Health Canada (from an acute study on volunteers), are in positive agreement with each other. However, a clear dose-response relationship may not be available based on the possible confounding factors of the studies as discussed in the following.

Table 2. Comparison of the US EPA RfC, Health Canada TC and WHO Air Quality Guideline for Toluene

Characteristics	US EPA (1992)	WHO (1987)	Health Canada (CEPA) (Environment Canada, 1992)
Study on which exposure limit is based.	Foo <i>et al.</i> (1990)	A number of available studies of occupationally exposed groups and controlled human exposure experiments.	Andersen <i>et al.</i> (1983)
Study type	Cross-sectional study of occupationally exposed workers	Both controlled experiments and epidemiological studies involving occupationally exposed workers	Controlled human exposure experiment
Study Population	30 female workers with no history of CNS disorders	Vary	16 healthy volunteers
Exposure Durations	8 hour/day, 5 days/week, duration not clear	Vary	6 hours/day for 4 days
Confounding Factors	Possibility of co-exposure to other solvent not addressed Controls matched for age, sex, race, medications; all are non-smokers and do not use alcohol	Vary Vary	Carefully controlled exposure to toluene only Individuals are randomly allocated to different exposure groups. 3 smokers reported; statistical analysis did not account for smoking

Table 2. Comparison of US EPA RfC, Health Canada TC and WHO Air Quality Guideline for Toluene (Contd.)

Characteristics	US EPA (1992)	WHO (1987)	Health Canada (CEPA) (Environment Canada, 1992)
Effects	Decrease in neurobehavioural function as measured by a number of tests;	Decrease in neurobehavioural functions and symptoms	Decrease in neurological functions as measured by a number of tests; increase in neurological symptoms and irritancy
Concentration-response relationship	Poor	Continuum of effects on the CNS with increase in toluene concentration	Clearly demonstrated
LOAEL (or LOEL) identified	332 mg/m ³ (332,000 µg/m ³)	375 mg/m ³ (375,000 µg/m ³)	375 mg/m ³ (375,000 µg/m ³)
NOAEL (or NOEL) identified	none	none	150 mg/m ³ (150,000 µg/m ³)
LOAEL/NOAEL (LOEL/NOEL) adjusted for continuous exposure	119 mg/m ³ (119 µg/m ³)	none	37.5 mg/m ³ (37,500 µg/m ³)
Modifying factors	300	50	10
Exposure limits	400 µg/m ³ (RfC)	7,500 µg/m ³ (air guideline)	3,750 µg/m ³ (TC)

The study of Foo *et al.* (1990), which the US EPA used for deriving the RfC, has a distinct drawback for assessing dose-response relationship for toluene. In the work environment of the study population, the possibility of co-exposure to other solvents that also cause CNS effects had not been addressed in the study and cannot be ruled out. The paucity of exposure information, and poor concentration-exposure relationship observed for each of the neurological tests administered to the workers, limit the usefulness of the study for characterizing the exposure limit.

In contrast, the Andersen study (Anderson *et al.*, 1983) that Health Canada relied on for the derivation of its TC was a well-controlled experiment on human subjects. In contrast to the occupational studies, exposures were limited to toluene specifically. Toluene concentrations for the exposures were carefully monitored and determined. A clear concentration-response relationship was demonstrated for all the neurobehavioural tests administered. Since volunteers were randomly allocated to different exposure groups, effects contributed by confounding factors, such as smoking, would likely occur in both control and experimental groups.

The inability of US EPA and WHO to identify a no-observed-effect level (NOEL) in the studies they have chosen is another deficiency in the derivation of criteria for toluene. Both agencies had to extrapolate a NOEL from LOEL by applying a safety/modifying factor. This procedure adds to the uncertainty of the resulting exposure limit values. On the other hand, Health Canada has chosen a study (Andersen *et al.*, 1983) that showed a clear concentration-effect relationship and a definite no-observed-effect level NOEL. Both these characteristics provide an overall confidence in the TC of this agency.

Although the exposure duration in the study of Anderson *et al.* (1983) is short (4-days only), the results would still be relevant to longer-term exposures, as several studies have indicated the absence of a duration-response relationship in toluene-induced neurotoxicity (US EPA, 1997). It is worth mentioning that Health Canada did not provide sufficient detail when explaining their rationale for the derivation of its TC, as well as in the critical analysis of the available data.

4.2.6 Discussion on Massachusetts Approach

Massachusetts used the US EPA RfC as a starting point for the derivation of their exposure limits - the Threshold Effects Exposure Limits (TEL) and Non-threshold effect exposure limit (NTEL). The TEL of $80 \mu\text{g}/\text{m}^3$ was derived by multiplying the RfC of $400 \mu\text{g}/\text{m}^3$ by a factor of 0.2 to account for the intake of toluene from air (i.e. as 20% of total intake from all media). According to the NPRI data, air emission accounts for over 99.7% of total toluene releases in Ontario. It would appear that inhalation will be the primary pathway of toluene exposure for people in Ontario. The Canadian federal government also reported that air exposure contributes to approximately 88-93% of the total daily intake of toluene (Environment Canada, 1992). The allocation of a default factor of 20 % to air will

overestimate the criterion by a very wide margin. This approach is therefore overly conservative and does not represent a typical exposure scenario in Ontario.

Although the Massachusetts Department of Environmental Protection (MDEP) reported that there was insufficient evidence to classify toluene's carcinogenic potential, they scored toluene as "C" for mutagenic potential, and "positive" for structure activity relationships. The mutagenic potential score was due to a positive finding in a mammalian polychromatic erythrocyte micronucleus test for chromosomal aberrations, as listed in the GENETOX database. (SAR) (MDEP, 1990). This combination of scores results in a non-threshold effects uncertainty factor (NTEUF) of 20. A NTEL of $20 \mu\text{g}/\text{m}^3$ is obtained by dividing the RfC of $400 \mu\text{g}/\text{m}^3$ by this uncertainty factor. No adjustment was made for multimedia considerations. The allowable ambient air limit (AAL) is set as the lower of the TEL or NTEL. Since the NTEL ($20 \mu\text{g}/\text{m}^3$) was lower, it was adopted as the AAL.

The study upon which the positive finding in GENETOX database is based, was confounded by co-exposure to benzene, which is a known bone marrow mutagen (GENETOX, 1997). The ACGIH concluded that reports of chromosomal aberrations and clastogenesis, following injection of toluene in rats and mice, have not been confirmed on further investigation (ACGIH, 1991). The weight-of-evidence indicates that toluene is not mutagenic in mammalian or microbial systems. In addition, there has been no evidence of carcinogenicity or mutagenicity for several of the metabolites of toluene (Environment Canada, 1992). Given this information, the mutagenicity assessment, the SAR scores, and the NTEUF derivation for toluene by Massachusetts are likely inappropriate.

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including toluene, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agencies that the Ministry considered appropriate for the development of air quality standards; and technical or economic impacts that may be anticipated consequent to the revision of the air quality standards.

During the consultation period the Ministry received four submissions from various stakeholders regarding the draft document for toluene. An automotive manufacturer suggested that the Ministry set a POI that is equivalent to Health Canada's Tolerable Concentration and that their facilities are operating at 80 % of the current POI. A stakeholder from the automobile equipment and parts industry indicated that the use of Health Canada's Tolerable Concentration does not represent a significant change from the current standard and therefore will probably not have an impact on this industry. A citizens group, concerned with emissions from a nearby plant, recommended the Ministry adopt the

RfC value from the US EPA for toluene. A stakeholder from the utility industry indicated that its emissions are well below the current standard and their facilities would be affected only if there were a drastic reduction from the current standard.

6.0 Overview of the Next Phase of the Ministry's Standards Setting Process

The stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information such on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding air quality standards for toluene.

7.0 Considerations in the Development of Air Quality Standards for Toluene

The current AAQC and half-hour POI standard for toluene have been determined to be $2,000 \mu\text{g}/\text{m}^3$, based on the odour effects of this compound. The odour effect and health effects of toluene on the central nervous system appear to be the most sensitive concerns. The odour detection thresholds for toluene range from 600 to $140,000 \mu\text{g}/\text{m}^3$, with a geometric mean of $6,000 \mu\text{g}/\text{m}^3$. The WHO has recommended an odour threshold of $1,000 \mu\text{g}/\text{m}^3$.

Short- or long-term exposure of humans or animals to toluene by inhalation can induce adverse central nervous system effects, and irritation and injury to the upper respiratory systems. At high concentrations toluene can induce liver and kidney toxicity, as well as adverse effects in developing fetuses. Considering these adverse health effects of toluene, most of the US State agencies and the Canadian federal health and environmental agencies have developed air quality criteria for the purpose of health protection.

The predominant health-based criteria are $400 \mu\text{g}/\text{m}^3$, $3750 \mu\text{g}/\text{m}^3$ and $7500 \mu\text{g}/\text{m}^3$, supported by separate health risk assessments provided by the US EPA, Health Canada, and the WHO, respectively. Among these three agencies, the quality of the study selected for health risk assessment

and the method of criteria derivation performed by Health Canada were considered to provide the most appropriate rationale and basis for criteria development.

The current Ontario POI standard should provide a sufficient margin of safety for the health effects of toluene, as well as be able to avoid the odour nuisance of this chemical.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the RfC of the US EPA, the Tolerable Concentration of Health Canada and the Air Quality Guideline of the World Health Organization. Of these, the Tolerable Concentration of 3,750 $\mu\text{g}/\text{m}^3$ developed by Health Canada is considered the most appropriate basis for air quality standards development. Deriving a 24-hour AAQC from the Tolerable Concentration will result in a criterion higher than the current Ontario odour-based 24-hour AAQC. Therefore, replacing the odour-based POI and 24-hour AAQC of 2,000 $\mu\text{g}/\text{m}^3$ is not recommended.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information and odour property, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for toluene:

- a 24-hour average AAQC of 2,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for toluene based on the odour nuisance and the adverse health effects of this compound; and,
- a half-hour average POI of 2,000 $\mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for toluene based on the odour nuisance of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the

submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards. In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of

cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE *Guideline F-14 (formerly 02-01), "Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;

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- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>*

Comments relevant to the setting of air quality standards for toluene can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The Reference Concentration (RfC) for toluene is reported as 0.4 mg/m³ (400 µg/m³). Toluene is not classifiable as to its human carcinogenic potential (Classification D). No air concentration guidelines exist for toluene.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

Key Reference(s):

Foo, S., J. Jeyaratnam and D. Koh, 1990. Chronic neurobehavioural effects of toluene. Br. J. Ind. Med. 47(7): 480-484.

NTP, 1990. Toxicology and carcinogenesis studies of toluene in F344/N rats and B6C3F1 mice (inhalation studies). National Toxicology Program, NTP-TR-371.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment for each chemical undergoes extensive internal and external scientific and policy reviews.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The inhalation RfC reported in IRIS was derived from two principal studies. The derivation of RfC assumes that a threshold exists for certain toxic effects. The RfC is "... an estimate of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime."

The derivation of the RfC considers portal-of-entry and systemic toxic effects.

Toluene is known to affect the central nervous system (CNS) and irritate the respiratory tract in humans. The US EPA (1997) reported that since the available studies could not provide sub-threshold concentrations (i.e. a no-observed-adverse-effect-level or NOAEL) for either of these effects, the Foo *et al.* (1990) study was used to develop the lowest-observed-adverse-effect-level (LOAEL) for CNS effects and the NTP (1990) study was used to develop the LOAEL for irritant effects.

Foo *et al.* (1990) conducted a cross-sectional study of 30 female workers exposed to toluene in an electronics assembly plant. Personal sampling devices were used to monitor exposure, which was reported as an 8-hour time weighted average (TWA). Exposed and control groups were matched for a number of confounding factors including age, ethnicity, use of medication, use of alcohol and smoking habits. Workers with prior histories of central or peripheral nervous system disorders were screened out of the study. Co-exposure to other solvents and prior exposure to toluene were not addressed or not provided. Air concentrations (TWA) for toluene were reported as 88 ppm (332 mg/m³) for the exposed workers and 13 ppm (49 mg/m³) for the control group. Neurobehavioural tests administered to both groups indicated that the control group performed better than the exposed group in all tests. Statistically significant differences were identified between the two groups' mean scores in 6 of the 8 tests administered. The US EPA has identified a number of limitations in this study. The limitations include an apparent lack of exposure information, a small cohort size, no consideration of irritant effects and no consideration of co-exposure to other solvents. Other carefully controlled clinical studies have, however, essentially confirmed the effects of toluene on the CNS, and have identified the absence of a duration-response relationship in the toluene-induced symptoms or effects. Foo *et al.* (1990) identified 88 ppm (332 mg/m³, assuming 25°C and 760 mm Hg) as a LOAEL for CNS effects based on an 8-hour TWA for the more highly exposed group of workers.

The NTP two year bioassay (1990) examined the effects of toluene exposure in Fischer 344 rats. Groups of rats (60 animals per sex per group) were exposed to 0, 600 or 1,200 ppm (0, 2,261 or 4,523 mg/m³) toluene vapours, 6.5 hours per day, 5 days per week for 103 weeks. Animals were sacrificed at 15 months and at the end of the studies for examinations. At both time points, statistically significant increases in the incidences of erosion of the olfactory epithelium and degeneration of the respiratory epithelium were observed in the exposed animals. Some female rats exposed to toluene at 600 and 1,200 ppm (2,261 and 4,523 mg/m³) exhibited a significant increase in inflammation of the nasal mucosa. From this study a LOAEL of 600 ppm (2,261 mg/m³) was determined for effects on

nasal epithelial tissue in both sexes. A NOAEL could not be derived from this study. However, a human equivalent concentration for the LOAEL was calculated to be 79 mg/m³. Several other human and animal studies summarized in the IRIS Inhalation RfC Assessment corroborate the neurotoxic and irritant effects of toluene (US EPA, 1997 and references therein).

The US EPA judged the CNS effects to be more severe than the irritant effects, and therefore, used the LOAEL from the Foo *et al.* (1990) study to derive the RfC. When converted to continuous exposure (assuming an occupational minute ventilatory volume of 10 m³/day and a daily minute ventilatory volume of 20 m³/day) the study LOAEL was adjusted by the US EPA as follows:

$$\begin{aligned}\text{Adjusted LOAEL} &= 332 \text{ mg/m}^3 \times (10 \text{ m}^3/\text{day} / 20 \text{ m}^3/\text{day}) \times (5 \text{ days}/7 \text{ days}) \\ &= 119 \text{ mg/m}^3\end{aligned}$$

An uncertainty factor (UF) of 300 was applied to the adjusted LOAEL derived from the Foo *et al.* study to account for intraspecies variability (i.e. to protect sensitive individuals, UF=10), for use of the LOAEL instead of a NOAEL (UF=10) and for database deficiencies (UF=3). As a result, the RfC was determined to be 400 µg/m³.

The US EPA has medium confidence in the study (Foo *et al.*, 1990) used to derive the RfC for toluene because of the lack of exposure data and the identification of only a LOAEL. Similarly, the NTP (1990) study which the US EPA considered was well conducted, but did not establish a NOAEL and was given a medium confidence rating. The overall database was considered by the US EPA to be incomplete in long-term human studies and not comprehensive with respect to reproductive/developmental studies. The database was also given a medium confidence rating. The RfC was given a medium confidence rating based on the study and database ratings.

9. Key Risk Management Considerations:

No information available.

10. Multimedia Considerations of Guidelines:

No adjustment for multimedia exposure is considered in the development of RfCs for threshold effects or unit risk values for non-threshold effects.

11. Other Relevant Factors:

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not have any specific air quality guideline for toluene. However, a risk-based reference exposure level (REL) of 200 $\mu\text{g}/\text{m}^3$ has been established for assessing non-cancer risk. The OEHHA has proposed a Chronic REL of 400 $\mu\text{g}/\text{m}^3$ and an acute REL of 37000 $\mu\text{g}/\text{m}^3$ recently.

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessment. These guidelines are prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider reference exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

5. *Documentation Available:*

California Air Resources Board (ARB), 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 893-895.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

Key Reference(s):

Nawrot, P.S., and R.S. Staples, 1979. Embryo-fetal toxicity and teratogenicity of benzene and toluene in mice. *Teratology*. 19:41A.

OEHHA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels - Toluene. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, USA.

OEHHA, 1998. Technical Support Document for the Determination of Acute Reference Exposure Levels for Airborne Toxicants - Toluene. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

6. Peer-Review Process and Public Consultation:

The California EPA has compiled Toxic Air Contaminant Identification Lists as part of the States' Air Toxic Program Assembly Bill (AB) - 1807. The document summarizes the general exposure and health effects of 224 substances identified in the list. The document also identifies the risk based guidance values which have been developed or adopted by the Office of Environmental Health Hazard Assessment. The draft document is currently undergoing an extensive peer-review and is open for public review and comments. To compile the technical summaries for the 244 substances identified, the existing governmental exposure and health effects databases (eg., HSDB, IRIS, etc.), and additional widely recognised reference texts were used.

The Reference Concentrations (RfCs), RELs and cancer potency values reported in both the draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted by the OEHHA after extensive review. The rationales for the derivation of all these values have undergone public review and consultation before finalization. Under the CAPCOA risk assessment process, each risk assessment is site specific. The exposed individuals should be notified when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input plays a key role in identifying and ranking facilities for risk assessment screening.

7. Status of Guideline:

Currently applied, however the REL is being revised.

8. Key Risk Assessment Considerations:

The chronic REL of 200 $\mu\text{g}/\text{m}^3$ was adopted from the Applied Action Level (AAL) established by the Department of Toxic Substances Control (DTSC) of the California EPA. AALs are developed in accordance with the California Site Mitigation Decision Tree as risk-based reference levels for human receptors (California EPA, 1997a). Levels are based on the toxicological and epidemiological literature available at the time of derivation (California EPA, 1997b). The AAL for toluene is based on a study by Nawrot and Staples (1979) which evaluated the developmental and reproductive toxicity of toluene in CD-1 mice (California EPA, 1997b). This study identified a subchronic lowest-observed-adverse-effects-level (LOAEL) of 0.78 $\mu\text{g}/\text{kg}/\text{day}$. Using an uncertainty factor of 10, this LOAEL was used to estimate a subchronic no-observed-adverse-effects-level (NOAEL) of 0.078 $\mu\text{g}/\text{kg}/\text{day}$. This

NOAEL was subsequently used to calculate the steady-state body-burden (SS_B) using the following equation (California EPA, 1997b):

$$SS_B = \frac{1.44 \times NOAEL \times t_{1/2}}{\text{Dosing Interval}} = 0.012 \mu\text{g/kg/day}$$

where: 1.44 is a unitless factor which relates the half-life of a compound to the first order elimination rate constant.
NOAEL = 0.078 $\mu\text{g/kg/day}$ (as determined above).
 $t_{1/2}$ (the half-life of toluene) = 2.63 hrs. (mice)
Dosing Interval = 24 hrs.

This SS_B was then adjusted by an uncertainty factor of 10 (to extrapolate from subchronic to chronic endpoints), and by an additional factor of 100 (to account for interspecies differences (extrapolating from animals to humans) and intraspecies variability (sensitive sub-populations)). From this adjusted SS_B , a total daily exposure, applied as a maximum exposure level (MEL), was calculated using the following equation (California EPA, 1997b):

$$MEL = \frac{SS_B \times \text{Dosing Interval} \times 70\text{kg}}{1.44 \times t_{1/2}} = 4.22 \text{ mg/m}^3 \text{ (4220 } \mu\text{g/m}^3\text{)}$$

where:
 $t_{1/2}$ = 3.4 hours (humans)
Dosing Interval = 24 hours
70 kg = average adult body weight

Since data on the absorption of toluene under steady-state conditions was not detailed in the literature, it was assumed that 100 % of the inhaled amount was absorbed. The AAL was calculated using the following equation:

$$AAL = MEL / 20 \text{ m}^3 \text{ (the daily respired volume)} = 211 \mu\text{g/m}^3$$

The DTSC rounded down this value to the final AAL 200 $\mu\text{g/m}^3$.

The OEHHA of the California EPA has recently proposed to adopt the RfC of 400 $\mu\text{g/m}^3$ developed by the US EPA, based on the central nervous effects of toluene. The California EPA is also proposing an acute REL of 37,000 $\mu\text{g/m}^3$, based on the central nervous system effects, eye, nose and respiratory irritation and reproductive and developmental effects.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways for a number of substances (specific compounds are listed under Table III-5 in CAPCOA, 1993). Toluene is not one of these substances.

11. *Other Relevant Factors:*

The AALs which were developed by the DTSC are no longer applied by the State, and have been replaced by Preliminary Remediation Goals (California EPA, 1997a). Therefore, the chronic risk-based reference value for toluene published in the CAPCOA document is out of date (California EPA, 1997b). The OEHHA acknowledges that the chronic REL which is reported in its risk assessment guidelines, is not current, and that they are in the process of revising the chronic reference level (ARB, 1997a). Although the REL reported under the current CAPCOA guidelines is out of date, it continues to be used as the chronic risk-based reference concentration upon which assessments of toluene are based, since the revised level is still under review (ARB, 1997a).

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Toluene (CAS# 108-88-3)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) for toluene is $80 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The Allowable Ambient Limit (AAL) for toluene is $20 \mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1988. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. . United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed scientific data and analyses from both public and government sources were used in the development of the Massachusetts ambient air guidelines. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. *Status of Guideline(s):*

Current. Guidelines may be updated periodically.

8. *Key Risk Assessment Considerations:*

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of toluene, an IRIS RfC was reported for this chemical. The MDEP, having reviewed the basis for the toluene RfC, has adopted the RfC, 0.4 mg/m^3 ($400 \text{ }\mu\text{g/m}^3$) as the starting point for the derivation of the MDEP air guidelines. Assuming that ambient air contributes only 20% of the total exposure, the RfC was divided by 5 to account for exposure through media other than air. The TEL was, therefore, calculated as $80 \text{ }\mu\text{g/m}^3$.

Non-Threshold Effects

The MDEP reported that there was insufficient evidence to classify toluene's carcinogenic potential (MDEP, 1990). However the MDEP, upon finding a positive result for mutagenic potential based on structure activity relationship (SAR) and in one positive test result in mammalian polychromatic erythrocyte micronucleus test for chromosomal aberrations listed in the GENETOX database, scored toluene as "C" for its mutagenic potential. Non-threshold effect exposure limit (NTEL) was developed by applying a non-threshold effect uncertainty factor (NTEUF) of 20 to the RfC ($400 \text{ }\mu\text{g/m}^3$) (MDEP, 1997). No adjustment was made for multimedia considerations. The resulting NTEL for toluene was calculated as $20 \text{ }\mu\text{g/m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Since the NTEL was lower, it was adopted as the AAL. The AAL for toluene is 20 $\mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive adverse health effect and is designed to protect the most sensitive individuals in the population. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less.

The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

In deriving the TEL factor guideline, a factor of 20% was applied to the RfC used as a relative source contribution factor, to allow for contributions from exposure media other than air. On the other hand, the AAL does not consider other sources of exposure.

11. Other Relevant Factors:

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)

3. *Guideline Value(s):* The initial Threshold Screening Level (ITSL) in Michigan is 400 mg/m³ (averaged over 24 hours).

4. *Application:*

Screening levels are health-based levels and are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules, as follows.

- i) Each source must apply the best available control technology for toxics (T-BACT);
- ii) After applying the T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRSL, and SRSL) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

US EPA, 1997. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, D.C.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL, including the US EPA's process for the development of reference concentrations (RfCs).

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves determination of an ITSL. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans.

The ITSL for toluene was adopted from the RfC developed by the US EPA. The ITSL, which is averaged over 24 hours, equals the inhalation RfC. For derivation of the US EPA RfC, please refer to Section 5.1, Federal Government of the United States.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.5 Agency-Specific Summary: State of New Jersey

1. Name of *Chemical*: Toluene (CAS # 108-88-3)

2. *Agency*: State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s)*:

The State of New Jersey has not set an air quality standard for toluene (NJDEP, 1997a). However, the State has adopted the United States Environmental Protection Agency's (US EPA) risk-based chronic reference concentration (RfC) of 400 $\mu\text{g}/\text{m}^3$ for toluene (NJDEP, 1997b).

4. *Application*:

The Air Quality Permitting Program (AQPP) requires the conduct of a risk assessment when applying for an air pollution control pre-construction permit. Depending on the type and size of the facility or sources, either one of the two approaches to risk assessment would be chosen. The two approaches are risk screening, conducted by the AQPP staff, and refined risk assessment completed by the applicant. A refined risk assessment is compulsory for certain categories of sources. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994).

5. *Documentation Available*:

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

Key Reference(s):

US EPA, 1997. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, D.C.

6. *Peer-Review Process and Public Consultation*:

None.

7. *Status of Guideline*:

Not applicable.

8. *Key Risk Assessment Considerations:*

The State adopted the US EPA's RfC of 400 $\mu\text{g}/\text{m}^3$ for toluene. This RfC is based on both central nervous system and respiratory irritation effects. The derivation of this RfC is detailed in section 11.1 Federal Government of the United States.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Toluene (CAS# 108-88-3)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC) for toluene is 45,000 $\mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) for toluene is 400 $\mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process for permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used by NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants, and to aid in the regulatory decision-making process using scientific data and professional judgement. However, these guidelines have not been subjected to the same degree of review as are applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

NYSDEC, 1997a. Letter to Sylvia Miedinger, GlobalTox International Consultants Inc., dated February 5, 1997. Subject: Rationale Documents requested for New York State air quality standards. Author: Thomas Gentile, Chief, Toxic Assessment Section, Bureau of Stationary Sources, Division of Air Resources. New York State Department of Environmental Conservation. Albany, New York.

Key Reference(s):

ACGIH, 1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices 1990-1991. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

US EPA, 1997. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington, D.C.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. *Status of Guideline(s):*

Current.

8. *Key Risk Assessment Considerations:*

Toluene is classified as a low toxicity air contaminant (Table IV, Appendix C of NYSDEC, 1991). Low toxicity air contaminants are defined as those chemicals for which irritation is the primary toxicological concern.

The SGC¹ was derived from the ACGIH (1991) occupational limit "Threshold Limit Value-Time Weighted Average" (TLV-TWA) by applying a factor of 4.2 to the TLV-TWA (188 mg/m³) to allow adjustment from an 8 hours/day, 5 days/week occupational exposure to a 24 hours/day, 7 days/week continuous exposure.

$$\text{SGC} = 188 \text{ mg/m}^3 / 4.2 = 44.8 \text{ mg/m}^3 = 45,000 \text{ }\mu\text{g/m}^3 \text{ (approximately)}$$

The New York state has adopted the US EPA's RfC of 0.4 mg/m³ (US EPA, 1997), to be the AGCs.

9. *Key Risk Management Considerations:*

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. *Multimedia Considerations of Guidelines:*

The NYSDEC guidelines consider only human exposure to contaminants in air.

¹In the process of reviewing and verifying the SGCs and AGCs, NYSDEC has confirmed that the 1991 "Air Guide - 1" document does not reflect the most recent guideline values or rationales (NYSDEC, 1997b). The criteria and rationales described here are correct.

11. *Other Relevant Factors:*

None.

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*

A guideline of 7.5 mg/m³ with a 24-hour averaging time is recommended. An odour detection threshold of approximately 1 mg/m³ with an averaging time of 30 minutes is also suggested as being appropriate as an air quality guideline.

4. *Application:*

The stated primary aim of the air quality guidelines is to "provide a basis for protecting public health from adverse effects of air pollution and for eliminating, or reducing to a minimum, those contaminants of air that are known or likely to be hazardous to human health and well being" (WHO, 1987). The guidelines are intended to provide background information and guidance to governments in making risk management decisions, particularly in setting standards. It is emphasized that the guideline values cited are not standards in themselves but a starting place which must be considered in the context of prevailing exposure levels and environmental, social, economic and cultural conditions. The air quality guidelines for non-carcinogens are intended to indicate levels combined with exposure times at which no adverse effect is expected to occur, or in the case of odorous compounds, will not create a nuisance of indirect health significance.

5. *Documentation Available:*

WHO, 1985. Environmental Health Criteria #52 - Toluene. International Programme on Chemical Safety, The World Health Organization, Geneva.

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No.

23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

Key reference(s):

Andersen, I., G.R. Lundqvist, L. Molhave, O.F. Pedersen, D.F. Procter, M. Vaeth, and D.P. Wyon, 1983. Human response to controlled levels of toluene in six-hour exposures. *Scandinavian J. of Work, Environment and Health*. 9:405-418.

Hellman, T.M. and F.H. Small, 1973. Characterization of petrochemicals odors. *Chemical engineering progress*, 69:75-77.

Naus, A., 1982. Olfactory thresholds of industrial substances. *Pracovni lekarstvi*, 34:217-2128.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific literature was utilized in the drafting of scientific background documents. These background documents were prepared by workgroups comprised of experts and submitted for internal review and external review to governments of Member States of the Region and to organizations and individuals engaged in air quality research or management.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

The WHO identifies air pollution as the major source of exposure to toluene and inhalation as the predominant route of exposure. The adverse human health effect of primary concern following exposure to toluene is dysfunction of the central nervous system (CNS).

The WHO concludes that there is a continuum of CNS effects in exposed humans, ranging from clearly adverse effects, such as confusion and muscle weakness, occurring at 750 mg/m³ and higher levels for very short periods, to slight changes in psychomotor function and mild symptoms detectable at 375 mg/m³ after exposure for periods of hours. Eye and nose irritation is detectable at 375 mg/m³ during a 6-hour exposure. Studies of occupationally exposed groups provide data reasonably consistent with those obtained from controlled acute human exposure experiments. The WHO states that the available data for animals and humans are inadequate for evaluating the carcinogenicity of toluene.

The lowest-observed-effect level (LOEL) identified by the WHO is 375 mg/m³ based on observations of the CNS effects and mucosal irritation. A "protection factor" of 50, with a 24-hour averaging time, is applied. This factor is judged to be adequate on considering the data on negative effects in humans, the lack of evidence of a chronic effect, and the minimally adverse nature of the observed effects at the LOEL. Dividing the LOEL by a factor of 50 gives the guideline level of 7.5 mg/m³ (7,500 µg/m³) for a 24-hour averaging time.

The WHO also identifies the odour detection threshold of approximately 1 mg/m³ (1,000 µg/m³) as possibly appropriate as an air quality guideline. No "protection factor" for a guideline based on the odour threshold would be necessary, however, an averaging time of 30 minutes is recommended to avoid complaints regarding odour.

9. *Key Risk Management Considerations:*

None.

10. *Multimedia Considerations of Guidelines:*

Human exposure to toluene from air, drinking water and food are described, however WHO has concluded that inhalation is the predominant route of exposure. No consideration for the potential for contribution from other sources is included in the guideline derivation.

11. *Other Relevant Factors:*

None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

The Netherlands has adopted a maximum immissible concentration (MIC) of 240 $\mu\text{g}/\text{m}^3$ (averaged over 3 hours) from the regional MIC developed by the province of Groningen. The MIC value is the maximum emission concentration of air pollution components in the outdoor air at the inhabited level.

4. *Application:*

Risk-based environmental quality objectives form the basis of the effects-oriented environmental policy. When these criteria are included in legislation, they become requirements that must be met. These effects-based criteria may be used simultaneously with source-oriented emission criteria which are the primary regulatory mechanisms in the Netherlands. If the effects-based criteria are exceeded, requirements may be imposed to lower the source-oriented emission criteria to bring the ambient levels to below the effects-based guidelines.

The Netherlands utilizes a progressive criteria setting process in implementing the effects-oriented policy. The objective is to reduce the emission of priority substances gradually to below a target value concentration. The policy defines a maximum permissible concentration based on toxicological evaluation and a negligible concentration which is set at 1/100 of the maximum permissible concentration. The negligible concentration is meant to be indicative of an environmental quality at which the risks of adverse effects are considered negligible. These risks apply to ecosystems, functional properties of the environment and other compartments. The target value is set to the negligible concentration or the naturally occurring background level. If the target value can only be met in a long term, intermediate objectives (limit or guidance values) will be used. In the course of time, the limit or guidance values will be tightened to reach the target value.

MIC values are regional air values originally developed in the province of Groningen. They have been adopted by the Netherlands. These values will be replaced gradually as the nation conducts extensive risk evaluation to derive national limit values for air.

5. *Documentation Available:*

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. *Peer-Review Process and Public Consultation:*

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

The regional MIC values were derived by the Province of Groningen from the occupational hygiene based national 1982-1983 Maximum Acceptable Concentration's (MACs) by applying a modifying factor. Since toluene is not considered a carcinogen, a factor of 150 was applied to the MAC ($375 \mu\text{g}/\text{m}^3$) to convert from a 40 hour work week occupational limit to an environmental MIC level to which the general population (children, adults and elderly) and all flora and fauna can be exposed 24 hours a day without being adversely affected.

9. *Key Risk Management Considerations:*

The national limit values are not based solely on health consideration, but rather include consideration of environmental, economic and social interests.

10. *Multimedia Considerations of Guidelines:*

None.

11. *Other Relevant Factors:*

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Toluene (CAS# 108-88-3)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

The Swedish Institute of Environmental Medicine has recommended air guideline values of 40-400 $\mu\text{g}/\text{m}^3$ (10-100 ppb) for toluene.

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not information available.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. For volatile aromatic hydrocarbons, such as toluene, xylene and styrene, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1,000.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

A detailed review of the basis of the Swedish guideline could not be conducted as the supporting documentation is available only in Swedish (Institute of Environmental Medicine, 1997).

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Toluene (CAS # 108-88-3)

2. *Agency:* Environment Canada/Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

Toluene was assessed under the first Priority Substance List (PSL1). No specific air quality guideline value has been identified for toluene. However, a risk-based tolerable concentration (TC) of 3,750 $\mu\text{g}/\text{m}^3$ was established for toluene.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada, 1992. *Canadian Environmental Protection Act* Priority Substances List Assessment Report - Toluene, Environment Canada, Health and Welfare Canada. Minister of Supply and Services Canada; Ottawa, Canada.

Environment Canada, 1993. *Canadian Environmental Protection Act* Priority Substances List Supporting Document: Toluene - *Unedited Document* Environment Canada and Health Canada.

Environment Canada, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA), Environment Canada, PSL2 Secretariat. October 1995.

Key Reference(s):

Andersen, I., G.R. Lundqvist, L. Molhave, O.F. Pedersen, D.F. Procter, M. Vaeth, and D.P. Wyon, 1983. Human response to controlled levels of toluene in six-hour exposures. *Scand. J. Work Environ. Health*, 9: 405-418.

6. *Peer-review Process and Public Consultation:*

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The TC is based on data presented in a clinical epidemiological study by Andersen *et al.* (1983) which investigated the neurological and respiratory irritation effects of toluene. This study examined the nasal mucus flow, lung function, subjective response and psychometric performance of 16 healthy male subjects reportedly exposed for 6 hours over 4 days to 0, 10, 40 or 100 ppm toluene under controlled conditions. Although the study reported that 3 of the subjects were smokers, the statistical analysis did not account for smoking. No other confounding variables were described in the study. At 100 ppm, irritation of the eyes and nose were noted. The subjects reported that tests were more difficult and strenuous during the 100-ppm exposure. Headaches, dizziness and a feeling of intoxication were significantly more often reported at 100-ppm. The exposures to 10 and 40 ppm did not result in any adverse effects. This study established a no-observed-effects-level (NOEL) in humans of 40 ppm (150 mg/m³). The TC was calculated using this NOEL, modified from a 6-hour daily dosing schedule to a 24-hour continuous exposure scheme, and adjusted by a factor of 10 to account for intraspecies variation. The mathematical manipulation resulted in a TC of 3.75 mg/m³ (3,750 µg/m³). No factor was included in the calculation of the TC to account for any database deficiencies.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours

TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours
TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
VINYLIDENE CHLORIDE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for which current air standards will be reviewed over the next several years. Vinylidene chloride was identified as a priority for review based on its pattern of use in Ontario and recent toxicological information that was published subsequent to the development of the existing standard in 1984. A review of scientific and technical information relevant to setting an ambient air quality standard for vinylidene chloride has been provided to stakeholders for comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for vinylidene chloride.

Vinylidene chloride (1,1-dichloroethene) is a volatile, colourless liquid with a "sweet" odour. It is synthesized on a large scale and co-polymerizes with other vinyl monomers, such as acrylonitrile, alkyl acrylates, and methacrylates. It is widely used in a number of commercial and industrial products such as flexible packing materials (e.g. Saran wrap), flame retardant coatings for carpets, and coatings for steel pipes.

Vinylidene chloride is not known to occur naturally in the environment, but can be found in landfills as a result of the breakdown of polyvinyl chloride. According to the National Pollutant Release Inventory (NPRI), there were no reported releases of vinylidene chloride between 1993 and 1997. There was only one Ontario facility reporting to NPRI on off-site transfers of vinylidene chloride between the reporting years of 1993 and 1995. Half-hour maximum concentrations of vinylidene chloride were found to be $0.81 \mu\text{g}/\text{m}^3$ at a hazardous waste facility, 0.25 to $0.65 \mu\text{g}/\text{m}^3$ in industrial areas, and 0.68 to $53.7 \mu\text{g}/\text{m}^3$ at landfills in the greater Toronto area. Ambient air levels of vinylidene chloride were measured in 1995 by Environment Canada. All the air samples showed concentrations of vinylidene chloride at or below the detection limit of $0.05 \mu\text{g}/\text{m}^3$.

There is little information regarding human exposure to vinylidene chloride. Odour thresholds from 400 to $4,000 \mu\text{g}/\text{m}^3$ have been reported. Short-term inhalation exposure to vinylidene chloride induces adverse neurological effects whereas prolonged exposure produces liver and kidney damage, eye, respiratory tract, and dermal irritation effects.

Vinylidene chloride has demonstrated carcinogenicity in mice and rats in chronic inhalation studies. Epidemiological studies on workers exposed to vinylidene chloride showed no statistically significant increase in cancer incidence. Vinylidene chloride is mutagenic in various bioassay systems, but generally requires a metabolic conversion to express its mutagenic properties. Based on carcinogenic evidence in animals, vinylidene chloride is classified as a 'possible human carcinogen' by the US EPA.

The US EPA has determined an inhalation unit risk of 5×10^{-5} per $\mu\text{g}/\text{m}^3$, based on statistically significant increases in kidney adenocarcinoma noted in male mice. The US Department of Human and Health Services (through the National Toxicology Program) and the State of California do not consider vinylidene chloride as a cancer-inducing agent. A reproductive study of vinylidene chloride demonstrated no effect on male fertility, but maternal toxicity and teratogenic effects were noted in offspring.

The current Ontario 24-hour AAQC for vinylidene chloride is $35 \mu\text{g}/\text{m}^3$ and the half-hour POI standard is $70 \mu\text{g}/\text{m}^3$, both of which were developed based on health concerns associated with this compound.

In revising the air quality standards of Ontario, the Ministry of the Environment is reviewing risk assessments and standards and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government. Most states have adopted the US EPA's cancer risk specific concentration of $0.02 \mu\text{g}/\text{m}^3$, based on an estimate of 1 in a million excess cancer risk for lifetime exposures, in the derivation of their long-term ambient air criteria. The current chronic inhalation Reference Exposure Level of the State of California is $32 \mu\text{g}/\text{m}^3$. Based on non-cancer adverse effects in the liver, California is proposing a REL of $20 \mu\text{g}/\text{m}^3$.

Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the lifetime cancer unit risk estimates of the US EPA and the chronic REL of the California EPA. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for vinylidene chloride based on the rationale of the current chronic REL of $32 \mu\text{g}/\text{m}^3$ from the California EPA. An additional margin of safety factor has been applied by the Ministry to this REL to limit exposure levels of vinylidene chloride considering its possible carcinogenic effect. As a result, a criterion of $10 \mu\text{g}/\text{m}^3$ is obtained and considered a 24-hour AAQC for Ontario.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for vinylidene chloride:

- **a 24-hour average AAQC of $10 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for vinylidene chloride based on the adverse health effects of this compound; and,**
- **a half-hour average POI standard of $30 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for vinylidene chloride based on the adverse health effects of this compound.**

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

-
- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Vinylidene chloride was identified as a priority for review based both on its pattern of use in Ontario and recent toxicological information that has been published subsequent to the development of the existing standard in 1970. A review of scientific and technical information relevant to setting an ambient air quality standard for vinylidene chloride has previously been provided to stakeholders for their comments. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour point of impingement (POI) standard for vinylidene chloride.

2.0 General Information

2.1 Physical and Chemical Properties

The following table provides some general information on Vinylidene chloride and its properties:

CAS #	75-35-4
RTECS #	KV9275000
UN #	UN 1303
Conversion Factors	1 ppm = 4 mg/m ³ or 4,000 µg/m ³
Boiling Point	31.7 at 760 mmHg
Flash Point	-16 °C (o.c.); -19 °C (c.c.)
Specific gravity	1.218 at 20/4 °C
Henry's Law Constant	0.19 atm-m ³ /mol
Log K _{ow}	1.32
Formula	C ₂ H ₂ Cl ₂
Molecular Weight	96.95
Vapour Density (air = 1)	-
Vapour Pressure	500 mmHg at 20 °C
Common Synonyms	1,1-dichloroethylene; 1,1-dichloroethene; VDC; 1,1-DCE; vinylidene dichloride

Vinylidene chloride is a colourless liquid. It is reported to have a mild, sweet odour resembling that of chloroform. The concentration at which its odour can be detected in air ranges from 400 to 4,000 µg/m³ (Clayton and Clayton, 1981; ACGIH, 1991; Verschueren, 1983; Cheminfo, 1996; CSST, 1997), though most reports list the odour detection threshold at approximately 2,000 µg/m³.

2.2 Uses of Vinylidene Chloride

Vinylidene chloride is synthesized on a large scale and is stabilized against oxidation and polymerisation by the addition of hydroquinone monomethyl ether. It copolymerises with other vinyl monomers, such as acrylonitrile, alkyl acrylates and methacrylates, vinyl acetate and vinyl chloride. It is widely used in a number of commercial and industrial products such as flexible packing materials (e.g. Saran wrap), flame retardant coatings for carpets and coatings for steel pipes.

2.3 Sources and Levels

Vinylidene chloride is not known to occur naturally in the environment, but can be found in landfills as a result of the breakdown of polyvinylidene chloride. It is produced by the dehydrochlorination of 1,1,2-trichloroethane by lime or sodium hydroxide (IARC, 1986; ATSDR, 1994).

The National Pollutant Release Inventory of Environment Canada does not indicate any releases of vinylidene chloride to the environment (air, water and soil) in reporting years of 1993, 1994, 1995, 1996 or 1997 (NPRI, 1993; NPRI, 1994; NPRI, 1995; NPRI, 1996; NPRI, 1997). Off-site transfers for containment of this compound, however, totalled 17 tonnes in 1993, 11.4 tonnes in 1994 and 21 tonnes in 1995. There is only one facility, located in Ontario, reporting to the NPRI on the transfers of vinylidene chloride.

Levels of vinylidene chloride are higher in areas surrounding production sites, which can be attributed to its release from industrial production and polymerisation processes (EPA 1977, 1985). Polymer synthesis and production facilities are the predominant contributors of vinylidene chloride emissions to the environment in North America (ATSDR, 1994). Vinylidene chloride is also found in the air around waste sites and sanitary landfills. The arithmetical mean concentration ranged from 1.56 to 156 $\mu\text{g}/\text{m}^3$ at five waste sites, and was 10.4 $\mu\text{g}/\text{m}^3$ near a sanitary landfill. The highest concentration measured at any of these six sites was 388 $\mu\text{g}/\text{m}^3$ (ATSDR, 1994).

In a study to determine indoor levels of vinylidene chloride, a total of 31 air samples (16 in summer and 15 in winter) were taken in 26 homes and apartments near Research Triangle Park, North Carolina. The reported mean levels of vinylidene chloride were 189 $\mu\text{g}/\text{m}^3$ for the summer and 28.4 $\mu\text{g}/\text{m}^3$ during the winter (US EPA, 1985). In only eight of the 31 samples, however, was any vinylidene chloride detected. Interestingly, the levels detected were higher than the outdoor ambient levels. This is probably due to the presence of vinylidene chloride in various products including; food-packaging films, adhesives, carpet backing, piping, and coating for steel pipes.

In a study of 18 Canadian cities, the average concentration of vinylidene chloride was found to range from 0 to 0.9 $\mu\text{g}/\text{m}^3$ (Dann, 1998). In only 10 of the 1440 samples was the vinylidene chloride concentration at, or slightly above, the detection limit. These ten samples were taken from eight different sites, with four sites located in Ontario (two in Toronto, and one each in Hamilton and Samia). Monitoring by the Ministry of Environment and Energy in Ontario found half-hour maximum concentration measurements of 0.81 $\mu\text{g}/\text{m}^3$ at a hazardous waste facility, 0.25 to 0.65 $\mu\text{g}/\text{m}^3$ in industrial areas, and 0.68 to 5.7 $\mu\text{g}/\text{m}^3$ at landfills in the greater Toronto area (MOEE, 1997). The detection limit for vinylidene chloride was approximately 0.02 $\mu\text{g}/\text{m}^3$.

From an analysis of recent applications for Certificates of Approval in Ontario, a sample of 6 facilities were identified with a Certificate of approval covering emissions of vinylidene chloride. The median Ground Level Concentration, estimated by Regulation 346 dispersion modelling, for all 6 sources was approximately $2 \mu\text{g}/\text{m}^3$, with a minimum of $0.3 \mu\text{g}/\text{m}^3$ and a maximum of $11.5 \mu\text{g}/\text{m}^3$.

2.4 Environment Fate

Vinylidene chloride is highly volatile. The atmospheric half-life of vinylidene chloride, following a reaction with hydroxyl radicals, was found to be 2 days (WHO, 1990). The products of this reaction are phosgene, formaldehyde and chloroacetyl chloride. Under aerobic conditions, such as those occurring in groundwater, vinylidene chloride is biotransformed into vinyl chloride. Volatilization is also the primary removal mechanism of vinylidene chloride from water. Photolysis, hydrolysis and oxidation are not significant processes in the transformation of vinylidene chloride. Vinylidene chloride does not significantly accumulate in aquatic environments with a bioaccumulation factor of 6.9 and a bioconcentration factor of 4 (Atri et al, 1985).

3.0 Toxicology of Vinylidene Chloride

The following toxicological review of vinylidene chloride is focusses primarily on inhalation, since this is the predominant pathway of human exposure. Data on other exposure media are included where relevant or where inhalation data are lacking.

The main target organs of the systemic effects of vinylidene chloride are the central nervous system, liver, kidney, and lung (ATSDR, 1994). Its toxicity is mediated by reactive metabolites, such as chloroacetyl chloride and monochloroacetic acid. These metabolites act at the cellular level, through the depletion of glutathione, to compromise the viability of the target tissue. For example, a reactive intermediate binds or alkylates hepatic macromolecules, leading to cell death. The metabolic pathways in rats and mice are similar, however, the greater rate of metabolism in mice, results in the formation of a greater concentration of toxic metabolites (reviewed in ATSDR, 1994). Based on the suggestion that formation of toxic metabolites is much less significant in humans, the American Conference of Governmental and Industrial Hygienists (ACGIH) views that vinylidene chloride poses substantially less risk to humans than it does to rodents (ACGIH, 1991).

Several groups of people are more sensitive to vinylidene chloride exposure. They include the very young, the elderly, pregnant women, those individuals with renal, cardiac or hepatic dysfunctions, and those who ingest large amounts of acetaminophen, alcohol, or phenobarbitals (ATSDR, 1994). A potential source of bioavailable vinylidene chloride is 1,1,1,2-tetrachloroethane. In the rat, it is readily converted to vinylidene chloride by reductive metabolism (Thompson *et al*, 1984).

3.1 Acute Toxicity

There is very little information regarding exposure to vinylidene chloride in humans. Short-term inhalation exposure to high concentrations of vinylidene chloride (around 4,000 ppm or 16,000 mg/m³) induce adverse neurological effects, including depression of the central nervous system which could lead to coma. It has been suggested that vinylidene chloride was transformed into another toxic agent within the body, for example dichloroacetylene, and it was this agent which produced these effects under particular work environments (ATSDR, 1994). Exposure to vinylidene chloride, at levels of 100,000 µg/m³, can lead to eye and upper respiratory tract irritation. These levels can also lead to irritation of the skin, though this may be due partly to the stabilizer (*p*-methoxyphenol) used in commercial grade vinylidene chloride (WHO, 1990).

Signs of central nervous system toxicity, such as depression, dyspnea, narcosis and death, have been observed following acute inhalation exposure to vinylidene chloride. These effects are similar across animal species (ATSDR, 1994).

3.2 Subchronic and Chronic Toxicity

Prolonged and repeated exposure to vinylidene chloride, below the odour threshold, may produce liver and kidney damage. Hepatotoxicity has been observed in workers exposed to vinylidene chloride for 6 years or less in a vinylidene chloride polymerization plant. More than half of the exposed workers had 50% or greater loss of liver function, as indicated by liver scans and measurement of liver enzymes (as reviewed in ATSDR, 1994). Liver is the major target organ in experimental animals of several species (monkeys, dogs, guinea pigs, rats and mice) (ATSDR, 1994; OEHA, 1997a). Animals exposed to continuous exposures are less tolerant than those exposed intermittently (ATSDR, 1994, OEHA, 1997a). The Agency for Toxic Substances and Disease Registry (ATSDR) has developed an intermediate minimum risk level (MRL) of 0.02 ppm (80 µg/m³). This was based on a NOAEL of 5 ppm (20,000 µg/m³) observed in guinea pigs exposed to 5, 15, 25 or 48 ppm (20,000, 60,000, 100,000 and 192,000 µg/m³) of vinylidene chloride for 24 hours per day over 90 days. Mottled livers were seen at 15 ppm (Prendergast *et al.* 1967, as cited in ATSDR, 1994).

In a chronic oral study (Quast *et al.* 1983, as cited in US EPA, 1998) rats were given vinylidene chloride in their drinking water, with an estimated average daily intake ranging from 7,000 to 20,000 µg/kg/day for males, and from 9,000 to 30,000 µg/kg/day for females. The results showed that chronic exposure to vinylidene chloride produced hepatic lesions with all treatment doses in females, but only at the highest dose level in males.

3.3 Reproductive and Developmental Toxicology

There is no information available regarding reproductive or developmental effects in humans from inhalation exposure to vinylidene chloride. Pre-mating exposure of male rats to 55 ppm (220 mg/m³) for 6 hours a day, 6 days a week, for 11 weeks did not affect fertility of the male rats and this concentration was considered a NOAEL (Short, *et al.*, 1977a). Similar results were observed in male mice exposed to vinylidene chloride at 10 or 30 ppm (40 or 120 mg/m³) 6 hours/day, 5 days/week; fertility was not adversely affected (Andersen and Jenkins, 1977).

Foetotoxic and developmental effects were found in a study by Short *et al.* (1977b, as cited in ATSDR, 1994) and Murray *et al.* (1979, as cited in ATSDR, 1994). A significant increase in the incidence of foetal skeletal anomalies was noted in the litters of rats exposed during pregnancy to 80 ppm (320 mg/m³) or in rabbits exposed to 160 ppm (640 mg/m³) (Murray *et al.*, 1979). Wavy ribs and delayed ossification in rat foetuses and skeletal alterations in rabbit foetuses were noticed. A NOAEL for developmental toxicity during continuous inhalation exposure was not identified. Prenatal exposure to vinylidene chloride at 15 ppm (60,000 µg/m³) resulted in soft tissue anomalies in rats and skeletal defects in mice, rats and rabbits (Short *et al.*, 1977b).

One study in humans suggests a link between neural tube defects in newborns from transplacental exposure to contaminated drinking water (NJDH, 1992, as cited in ATSDR, 1994). Nitschke *et al.* (1983, as cited in ATSDR, 1994) conducted a three-generation reproductive study on rats, administering vinylidene chloride in drinking water at 30 mg/kg/day or less. The results showed that there was no exposure-related effect on reproduction or neonatal development. The US EPA (1998) states that vinylidene chloride is foetotoxic but not teratogenic.

3.4 Genotoxicity

Vinylidene chloride has demonstrated positive mutagenic activity in several genetic toxicology assays spanning several phylogenetic groups (ATSDR, 1994). However, these results usually require metabolic activation. Mutagenic properties have been found in bacteria and yeast. It Vinylidene chloride induced gene conversion in yeast, chromosome aberrations and sister chromatid exchange in cultured mammalian cells, and DNA damage in mice *in vivo*. There is no direct evidence that exposure to vinylidene chloride causes genotoxic effects in humans. There is, however, some evidence that it can be activated into toxic metabolites by human liver cells, only in the presence of post-mitochondrial S9, to induce mutagenic responses in *Salmonella* (ATSDR, 1994). This suggests that human liver is capable of activating vinylidene chloride into mutagenic metabolites.

A strong mutagenic response was observed in the prokaryotes *Salmonella typhimurium* and *Escherichia coli*, while with a lower eukaryote, *Saccharomyces cerevisiae*, the mutagenic response

from two distinct tests were both marginal. For the above organisms, a metabolic activation system was required suggesting that vinylidene chloride action is mediated by metabolites. Vinylidene chloride induced gene mutations in *Tradescantia*, but not in *in vitro* tests with Chinese hamster V79 cells at the hypoxanthine guanine phosphoribosyl transferase locus, nor with chromosome aberration studies on Chinese hamster cells. In addition, no activity was shown *in vivo* in either the induction of chromosomal aberrations in mouse bone marrow, or in the dominant lethal assay in CD rats. However, vinylidene chloride induced both an unscheduled DNA synthesis (UDS) response in primary rat liver hepatocytes *in vitro* (WHO, 1990), as well as an UDS response in mice *in vivo*. These data indicate that vinylidene chloride is a mutagen that lacks clastogenic properties as it does not appear to induce chromosome aberrations either *in vitro* or *in vivo*.

3.5 Carcinogenicity

No causal relationship has been established between occupational exposure to vinylidene chloride and incidence of cancer in workers. This is based on data from epidemiological studies on workers occupationally exposed to vinylidene chloride in a rubber plant (Waxweiler, 1981), and in a production and polymerisation plant (Ott *et al.*, 1976). However, the results of these studies may not be reliable or appropriate based on the small cohort size used and the short duration of time for which the workers were observed. In addition, the potential risk may be underestimated because no allowance was made for a latency period. There was also no statistically significant increase in cancer incidence associated with exposure to vinylidene chloride in these studies.

Results of vinylidene chloride carcinogenicity in animals have been inconsistent. Positive correlation between exposure to vinylidene chloride and tumour incidence was observed in one inhalation study in which male and female Swiss mice were exposed to either 10 or 25 ppm (40,000 or 100,000 $\mu\text{g}/\text{m}^3$) of vinylidene chloride, 4-5 days per week for 12 months (Maltoni, *et al.*, 1985, as cited in ATSDR, 1994; US EPA, 1998). A statistically significant increase in kidney adenocarcinoma incidence was observed in male mice, and in pulmonary adenoma incidence in both male and female mice. A statistically significant increase in mammary carcinomas was also noted in female mice, but no clear dose-response relationship was observed. Similar results were observed in Sprague-Dawley rats exposed to 10 to 150 ppm (40,000 to 600,000 $\mu\text{g}/\text{m}^3$) of vinylidene chloride for the same exposure schedule (4-5 days per week for 12 months) (Maltoni, *et al.*, 1985, as cited in US EPA, 1998). A statistically significant increase in total mammary tumours (not carcinoma alone) was noted, but no dose-response relationship was observed.

The results of other inhalation exposure studies with mice and rats were negative with regard to the carcinogenic activity of vinylidene chloride (ATSDR, 1994; US EPA, 1998). These studies suffer from procedural weaknesses and lack of conclusive results. For example, none of the inhalation studies were longer than 12 months in duration, and most did not use exposures up to the maximum tolerated

dose (MTD). In addition, the observed increase in tumour incidence was either not statistically significant or, when observed, did not demonstrate a clear dose-response relationship.

Among the available animal studies with exposure to vinylidene chloride by the oral route, positive findings were obtained only in a two-year drinking water study from the National Toxicology Programme (NTP) (NTP, 1982 as cited in ATSDR, 1994 and US EPA, 1998). Male Sprague-Dawley rats that were exposed to vinylidene chloride administered in drinking water at 5 mg/kg/day (the highest dose) for two years developed adrenal pheochromocytomas. However, the increase in the incidence of adrenal tumours was not statistically significant when compared with control animals. Most other oral studies were carried out at doses below the maximum tolerated dose, animals were exposed for 12 months or less (less than lifetime) and results were mostly negative. Therefore, these oral studies suffer from the same deficiency in reliable results as those observed in the inhalation studies discussed earlier.

Vinylidene chloride was not considered a complete carcinogen when applied topically or subcutaneously to Swiss ICR/Ha mice. However, it acted as an initiator if animals were subsequently exposed to phorbol myristate acetate, a tumour promoter (Van Duuren *et al.*, 1979 as cited in US EPA, 1998 and ATSRD, 1994).

3.6 Environmental Effects

There are no data on the effects of vinylidene chloride on terrestrial wildlife. Fumigation of hybrid clones of spiderwort (*Tradescantia*) at 88 mg/m³ for 24 hours or 5,152 mg/m³ for 6 hours did not cause inactivation of the dominant gene (Chieco *et al.*, 1982).

Vinylidene chloride is moderately toxic to aquatic organisms. Ninety-six-hour LC₅₀ values for fish range from 74 mg/L (static system with capped jars) (Buccafusco *et al.*, 1981) to 220 mg/L (static, open system) for bluegill sunfish (*Lepomis macrochirus*) (Dawson *et al.*, 1977). The water flea, *Daphnia magna*, is the only freshwater invertebrate for which vinylidene chloride toxicity information is available; 48-hour LC₅₀ values range from 11.6 mg/L (US EPA, 1985) to 79 mg/L (LeBlanc, 1980). A sub-acute exposure of Sheepshead minnows (*Cyprinodon variegatus*) to vinylidene chloride under flow-through conditions resulted in a 13-day LC₅₀ of 29 mg/L (US EPA, 1985). The 96-hour median effective concentration (EC₅₀) for freshwater algae (*Selenastrum capricornutum*) was found to be greater than 798 mg/L vinylidene chloride (US EPA, 1985); the endpoint in the study was reduction in cell number.

4.0 Existing Ambient Air Quality Criteria

4.1 Overview

Currently, the Ontario Ambient Air Quality Criterion (AAQC) for vinylidene chloride is $35 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time, established on the basis of liver injury; the half-hour point of impingement (POI) guideline is $70 \mu\text{g}/\text{m}^3$, established on the basis of liver injury and the consideration of the potential mutagenic and carcinogenic effects of this compound (MOEE, 1994a).

The documentation for ten agencies, including the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government, was reviewed for the existence and basis of air quality criteria for vinylidene chloride. A brief summary of this review is presented in Table 1, and agency-specific summaries of information concerning air quality guidelines for vinylidene chloride are presented in Section 11.0 of the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

The US EPA (1985; 1998) has classified vinylidene chloride as a 'possible human carcinogen' and reports an inhalation unit risk of 5×10^{-5} per $\mu\text{g}/\text{m}^3$. Based on this estimate, a lifetime exposure to $0.02 \mu\text{g}/\text{m}^3$ of vinylidene chloride may increase the incidence of cancer at a risk level of 1 in 1,000,000. Most of the U.S. state agencies have derived their air quality criteria based on the carcinogenic potential of vinylidene chloride. Massachusetts, Michigan, New Jersey, and New York adopted the risk-specific level of $0.02 \mu\text{g}/\text{m}^3$ (at 1 in a million lifetime cancer risk), developed by the US EPA, for either their annual or lifetime exposure guidelines. The State of California does not consider vinylidene chloride a potential carcinogen, but derived its chronic reference exposure level (REL) of $32 \mu\text{g}/\text{m}^3$ from the non-cancer reference dose level (RfD) of $9 \mu\text{g}/\text{kg}/\text{day}$ developed by the US EPA. The State of California is proposing to revise its chronic REL to $20 \mu\text{g}/\text{m}^3$, based on the liver toxicity of this compound (OEHHA, 1997a). The Netherlands has a maximum concentration of $200 \mu\text{g}/\text{m}^3$ and a negligible concentration of $2 \mu\text{g}/\text{m}^3$.

Table 1. Summary of Existing Air Quality Guidelines¹ for Vinylidene Chloride

Agency	Guideline Value	Basis of Guideline	Date ²	Comments
USEPA (IRIS)	9 µg/kg/day (reference dose level)	Rat oral chronic RfD	1992	LOAEL (HEC) adjusted with uncertainty factors (hepatic lesions)
	0.02 µg/m ³ (lifetime exposure)	Chronic inhalation 12-month study in mice; kidney adenocarcinoma	1992	1*10 ⁻⁶ additional cancer risk
	0.2 µg/m ³ (lifetime exposure)			1*10 ⁻⁵ additional cancer risk
California (CAPCOA)	32 µg/m ³ (Inhalation chronic annual)	Reference concentration RfD 9 µg/kg/day Liver toxicity in guinea pigs	1993	Non-cancer Reference Exposure Level (Chronic annual) US EPA IRIS GI and liver end-points
	Proposed: 20 µg/m ³ (Inhalation chronic annual)			
Massachusetts	0.02 µg/m ³ (annual average ambient level)	Chronic inhalation 12-month study in mice; kidney adenocarcinoma	1991	Threshold and non-threshold effects
	1.08 µg/m ³ (24 hour exposure)	Occupational exposure	1991	TEL ACGIH
Michigan	0.02 µg/m ³ (lifetime exposure; IRSL) 0.2 µg/m ³ (SRSL)	Chronic inhalation 12-month study in mice; kidney adenocarcinoma	1995	Annual average IRSL; US EPA 1*10 ⁻⁶ additional cancer risk
New Jersey	0.02 µg/m ³ (lifetime exposure - based on IRIS)	Chronic inhalation 12-month study in mice; kidney adenocarcinoma	1994	1*10 ⁻⁶ additional cancer risk; U.S.EPA carcinogen class: C
New York	0.02 µg/m ³ (annual - AGC)	Chronic inhalation 12-month study in mice; kidney adenocarcinoma	1994	Chronic annual; 1*10 ⁻⁶ additional cancer risk; US EPA
	2000 µg/m ³ (1-hour average - SGC)	Occupational exposure limits	1994	Acute 1-hour average; based on ACGIH TLV-TWA
WHO	none		1987	No value found
The Netherlands	200 µg/m ³ (max. permissible conc.) 2 µg/m ³ (negligible conc. NC)	Chronic monkey study - Liver histopathology	1993	NOAEL adjusted with UF; no target or limit value specified
Sweden	none		1993	No value found
Canada (CEPA)	none		1993	Not in PSL-1 or PSL-2

Ontario	35 µg/m ³ (24 hour average)	Health	1984	24-hour averaging time: Ambient Air Quality Criterion
	70 µg/m ³ (half-hour POI)	Health	1984	Point Of Impingement guideline

1. Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
2. Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.

In addition to long-term criteria, some states have established short-term limits based on occupational standards. Massachusetts divided the TLV-TWA of 20,000 µg/m³ of the ACGIH by a factor of 18,375, to get a 24-hour criterion (threshold effect level) of 1.08 µg/m³. New York State used the TLV-STEL of 79,000 µg/m³ from the ACGIH to derive its Short-Term Guideline Concentration (SGC) of 2,000 µg/m³.

Workplace exposure limits have been established by different agencies. The Occupational Safety and Health Association (OSHA) has set the legal airborne Permissible Exposure Limit - Time Weighted Average (PEL-TWA) at 4,000 µg/m³ over an 8-hour work shift (ACGIH, 1991). The National Institute of Occupational Safety and Health (NIOSH) has classified vinylidene chloride as a potential occupational carcinogen, but has not set either an airborne Recommended Exposure Limit (REL), or an Immediately Dangerous to Life or Health (IDLH) value (NIOSH 1994).

The American Conference of Governmental Industrial Hygienists (ACGIH) has set a Threshold Limit Value - Time Weighted Average (TLV-TWA) at 20,000 µg/m³ and a Short-term Exposure Limit of 79,000 µg/m³ (ACGIH, 1996), based on the hepatic effect of vinylidene chloride.

4.2 Evaluation of Existing Criteria

Exposure to vinylidene chloride may induce liver tissue lesions and possibly result in an increased incidence of tumour development in the kidneys or the adrenals. Considering these health effects, most of the U.S. agencies have established air quality criteria based on both the carcinogenic and non-carcinogenic effects of vinylidene chloride. The following will provide a brief review of the rationales for these criteria.

Approaches Based on a Carcinogenicity Endpoint

Several agencies have evaluated the cancer effects of vinylidene chloride. The U.S. National Toxicology Programme concluded there was no evidence of carcinogenicity in rats and mice exposed to vinylidene chloride by gavage (NTP, 1982). The International Agency for Research on Cancer (IARC) concluded that there was insufficient data to evaluate vinylidene chloride, and considered it 'not classifiable as to human carcinogenicity' (IARC, 1979). The US EPA has classified vinylidene chloride as a 'possible human carcinogen', based on limited evidence of carcinogenicity in animals and inadequate evidence in humans (US EPA 1998).

The US EPA (1985; 1998) determined an inhalation unit risk for vinylidene chloride of 5×10^{-5} per $\mu\text{g}/\text{m}^3$ (equivalent to 1 in 100,000 excess cancer risk at a lifetime exposure to $0.2 \mu\text{g}/\text{m}^3$). This was based on an one-year mouse inhalation exposure study reported by Maltoni *et al.* (1985), using the linearised multistage procedure. Human equivalent doses were determined assuming 0.035 kg as the average weight of male mice and adjusting for a continuous lifetime exposure, 70 kg weight and 1.85 m^2 surface areas for humans. A slope factor of $0.2 \text{ mg}/\text{kg}/\text{day}$ was calculated using estimated administered doses of 40,000 or 100,000 $\mu\text{g}/\text{m}^3$. Confidence in the inhalation risk estimates was described rather than rated; a sufficient number of animals were used, but, the study duration was only for 50% of lifetime, and only two dose points provided suitable data for analysis (US EPA, 1998).

The US EPA supports its cancer assessment by noting that in a second experiment performed by Maltoni *et al.* (1985), although a clear dose-response relationship was not observed, Sprague Dawley rats showed a statistically significant increase in total mammary tumours. Vinylidene chloride acted as an initiator when applied to skin in mice. Other data supporting the carcinogenicity of vinylidene chloride include mutagenicity data, and the similarities in structure between vinylidene chloride and vinyl chloride, a known carcinogen. Although most other studies have given negative results for carcinogenicity, most suffer from methodological limitations (US EPA, 1998).

Based on the NTP (1982) study which showed a non-significant increase in the incidence of pheochromocytomas in male rats, the US EPA derived an oral cancer slope factor of $0.6 \text{ per mg}/\text{kg}/\text{day}$ (US EPA, 1998).

Approaches Based on a Non-carcinogenic Endpoint

The US EPA inhalation reference concentration (RfC) is currently under review. The US EPA (1998) has calculated an oral Reference Dose (RfD) of $9 \mu\text{g}/\text{kg}/\text{day}$ for vinylidene chloride. This was derived from the LOAEL of 50 ppm ($9 \text{ mg}/\text{kg}/\text{day}$) for hepatic lesions observed in the rat chronic oral study of Quast *et al.* (1983, as cited in US EPA, 1998). The RfD was calculated by the application of a total

uncertainty factor of 1,000, resulting based on an uncertainty factor of 10 for the use a LOAEL rather than a NOAEL, 10 for interspecies variation and 10 for the protection of sensitive human subpopulations.

California derived an inhalation reference exposure level (REL) of $32 \mu\text{g}/\text{m}^3$, based upon the US EPA's RfD. Recently, California has proposed a revised REL of $20 \mu\text{g}/\text{m}^3$ (OEHHA, 1997a). This is based on an observed NOAEL of $20 \text{ mg}/\text{m}^3$ for hepatic necrosis and fatty infiltration in guinea pigs, from a 90-day inhalation study by Prendergast *et al.* (1967, as cited in OEHHA, 1997a). The NOAEL of $20 \text{ mg}/\text{m}^3$ was divided by an uncertainty factor of 1000, 10 for the use of a subchronic study rather than a chronic study, 10 for variation among species, and 10 for variation within species. These uncertainty factors were judged to be appropriate since there is a limited number of subchronic and chronic inhalation studies, limited evidence in human studies which suggest an association with liver damage in humans, and no metabolism data in humans.

5.0 Status of Stakeholder Consultation

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including vinylidene chloride, for air quality standards development under the Standards Plan (MOEE, 1996). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry; the rationale of the agency guidelines of which the Ministry has considered appropriate for the development of air quality standards; issues whether vinylidene chloride should be considered a carcinogen or non-carcinogen, and; technical and economic impacts that may be anticipated consequent to the revision of the air quality standards.

During the consultation period, the Ministry received two submissions from stakeholders regarding the draft document for vinylidene chloride. A stakeholder (environmental engineering) commented on the appropriateness of the scientific rationale assessed for Ontario and suggested that there was not enough scientific evidence to consider this compound a human carcinogen. Comments from a public utility stakeholder indicated that the facility would have no problem meeting a lowered standard.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

Stakeholders' comments received during the first phase of the standards development process (information drafts) were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard, is now complete. During this initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard, which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the levels of the air quality standard for vinylidene chloride. If the proposed standard cannot be achieved immediately, this phase will be followed by a third phase in which risk management options will be discussed with stakeholders. A risk management phase will involve careful consideration of human and ecosystem health benefits and stakeholder input regarding the economic impacts and technical feasibility of achieving the standard. In some cases, the Ministry may propose an interim POI standard to ensure continued environmental improvement while the risk management phase proceeds.

7.0 Considerations in the Development of Air Quality Standards for Vinylidene Chloride

The current Ambient Air Quality Criterion (AAQC) for vinylidene chloride in Ontario is $35 \mu\text{g}/\text{m}^3$ for a 24-hour averaging time. The half-hour POI guideline is $70 \mu\text{g}/\text{m}^3$. These criteria were established based on the adverse health effects of vinylidene chloride, the potential mutagenic and carcinogenic effects of this compound were also considered.

Inhalation of vinylidene chloride at high concentrations may result in neurological effects such as depression and possibly coma. In animals, the most commonly observed adverse effect from long-term inhalation exposure is liver damage, such as hepatic necrosis and fatty infiltration. Kidney damage has also been noticed. Environmental agencies and occupational health and safety agencies have derived exposure limits based on the hepatic effect of vinylidene chloride. The current chronic REL of the California EPA is $32 \mu\text{g}/\text{m}^3$. This agency is proposing to revise its chronic inhalation REL to $20 \mu\text{g}/\text{m}^3$, based on the necrotic effect of vinylidene chloride in the livers of animals. This proposed REL is currently under public review.

Chronic exposure to vinylidene chloride may also induce development of cancer in animals. There is also evidence that this compound may be genotoxic, as positive mutagenic assay results have been observed in some bacteria and some animal liver cells. Concerns regarding the carcinogenic potential of vinylidene chloride have led US agencies, such as the US EPA, agencies of the states of Massachusetts, Michigan, New Jersey and New York, to develop cancer-based exposure limits. These agencies estimate that inhalation exposure to vinylidene chloride at $0.02 \mu\text{g}/\text{m}^3$ for a lifetime may result in an additional cancer risk of one in a million. The IARC and the California EPA do not consider the carcinogenicity of vinylidene chloride a significant endpoint.

There is no substantiated evidence to warrant a carcinogenic endpoint in the development of an AAQC and POI standard for Ontario. This consideration is based on a high degree of uncertainty associated with the risk assessment for this compound. The uncertainty arises from the lack of reliable human data

for a detailed risk assessment, the lack of clear genotoxic effects, the diversity and severity of adverse effects observed in animals exposed to vinylidene chloride, particularly the inconsistent carcinogenicity findings in animals, and the discrepancy among various agencies to embark on cancer and noncancer-based approaches for their criteria development.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific studies which support the development of the lifetime cancer unit risk estimates of the US EPA and the chronic REL of the California EPA. After reviewing additional toxicological information, the Ministry has decided to derive air quality standards for vinylidene chloride based on the rationale for the current chronic REL of $32 \mu\text{g}/\text{m}^3$ from the California EPA. In view of the possible carcinogenic effect of vinylidene chloride, an additional margin of safety factor of 3 has been applied to this REL in an attempt to limit exposure levels of this compound. As a result, a criterion of $10 \mu\text{g}/\text{m}^3$ is obtained. Since the REL is derived from the RfD of the US EPA, it is appropriate to consider for a 24-hour averaging exposure period and therefore the criterion of $10 \mu\text{g}/\text{m}^3$ can be used as a 24-hour AAQC. The Ministry of the Environment uses a factor of 3 to convert from criteria based on 24-hour average concentrations to half-hour POI standards. This factor is derived from empirical measurements and is selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). Accordingly, a half-hour POI of $30 \mu\text{g}/\text{m}^3$ has been obtained.

In summary, based on the information reviewed from leading agencies and the assessment of toxicological information, the Ministry is proposing the following Ambient Air Quality Criterion and Point Of Impingement standard for vinylidene chloride:

- a 24-hour average AAQC of $10 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for vinylidene chloride based on the adverse health effects of this compound; and,
- a half-hour average POI standard of $30 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for vinylidene chloride based on the adverse health effects of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above

recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;
2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in

accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects" Economic Services Branch- April 1994*, and;

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- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards." Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>*

Comments relevant to the setting of air quality standards for vinylidene chloride can be sent to:

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* US Environmental Protection Agency

3. *Guideline Value(s):*

No ambient air exposure limits are currently promulgated. The reference dose for chronic oral exposure (RfD) on the basis of a 2-year rat study is listed as 9 µg/kg/day in the IRIS database (US EPA, 1998; last review 08/15/92). Vinylidene chloride is classified as a possible human carcinogen (C) with a unit risk from inhalation exposure of 5×10^{-5} per µg/m³. The linearised multistage extrapolation method was used.

4. *Application:*

IRIS was developed as a source of consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines on their own. IRIS also contains a summary of current American government regulatory actions under various mandates.

5. *Documentation Available:*

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Key Reference(s):

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6. *Peer Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the EPA and within other science-based US regulatory agencies. Information is put on IRIS after results of the public review and comments on draft documents/information have been addressed.

7. *Status of Guideline:*

No current guidelines exist for vinylidene chloride.

8. Key Risk Assessment Considerations:

An epidemiological study by Ott *et al.* (1976) was found to be inadequate to assess human cancer risk from vinylidene chloride. No exposure associated increase in carcinogenicity was observed in workers. The US EPA (1998) has calculated an inhalation cancer risk based on a 12-month inhalation study by Maltoni *et al.* (1985) using Swiss mice. In the study, male and female Swiss mice were exposed to 40,000 and 100,000 $\mu\text{g}/\text{m}^3$ of vinylidene chloride for 4-5 days per week for 12 months. A statistically significant number of kidney adenocarcinomas were observed in male mice. Also, statistically significant numbers of mammary carcinomas in female mice and pulmonary adenomas in mice of both sexes were observed, but no clear dose-response relationship was observed. In another study by Maltoni *et al.*, Sprague-Dawley rats were similarly exposed to doses of vinylidene chloride ranging from 40,000 to 600,000 $\mu\text{g}/\text{m}^3$. A significant increase was noted in total mammary tumours but not in carcinomas alone. An NTP study conducted with Sprague-Dawley rats for a duration of 2 years also had shortcomings: the highest dose tested was not the maximum tolerated dose, and a non-statistically significant increase in male rat adrenal tumours was noted. Nonetheless, the US EPA derived a cancer slope factor of 0.6 per $\text{mg}/\text{kg}/\text{day}$ based on these results. Confidence in this risk estimate is strengthened since the slope factor using these two studies are within a factor of 2 of each other.

The US EPA (1998) calculated the Reference Dose (RfD) for vinylidene chloride from the rat chronic oral study of Quast *et al.* (1983) to be 9 $\mu\text{g}/\text{kg}/\text{day}$. Rats were given vinylidene chloride in their drinking water with an estimated average daily intake of 7,000, 10,000 and 20,000 $\mu\text{g}/\text{kg}/\text{day}$ for males and 9,000, 14,000 and 30,000 $\mu\text{g}/\text{kg}/\text{day}$ for females, where Sprague-Dawley rats were exposed to 44,000 and 176,000 $\mu\text{g}/\text{m}^3$ of the compound. The results showed that chronic exposure to vinylidene chloride produced hepatic lesions in all treatment doses in female rats, but only at the highest dose level in male rats. This study is considered to be a more suitable model for human exposure than the NTP study where the animals were treated by gavage. The RfD was calculated from the rat oral LOAEL (HEC) (Lowest Observed Adverse Effect Level - Human Equivalent Concentration) by the application of uncertainty factors: 10 for use of a LOAEL; 10 for interspecies variability; and 10 for the protection of sensitive individuals. The RfD is under review.

9. Key Risk Management Considerations:

None, since no guidelines for ambient air exist.

10. Multimedia Considerations of Guidelines:

The oral drinking water unit cancer risk for vinylidene chloride is reported at $1.7 \times 10^{-5} \mu\text{g}/\text{m}^3$. The oral slope factor was calculated as 0.6 per $(\text{mg}/\text{kg})/\text{day}$. The ambient water quality criteria for freshwater aquatic organisms show the acute LEC to be 11,600 $\mu\text{g}/\text{L}$ and the acute LEC for marine organisms to be 224,000 $\mu\text{g}/\text{L}$.

11. Other Relevant Factors:

No information.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* State of California (Office of Environmental Health Hazard)

3. *Guideline Value(s):*

The non-cancer reference exposure level (REL) for inhalation is $32 \mu\text{g}/\text{m}^3$ and has been adopted from the US EPA IRIS database. Vinylidene chloride is listed as a substance for which emissions must be quantified. A revised chronic REL of $20 \mu\text{g}/\text{m}^3$ is being proposed.

4. *Application:*

"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' program." (CAPCOA, 1993). This program is based on a California State Law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et Seq.*). The act specifies how local Air Pollution Control Districts determine which facilities in the area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritized. These Guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and re-submission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

Several studies have reported the subchronic or chronic toxicity of vinylidene chloride in laboratory animals. This indicate that the liver is the primary target organ. The principal study used on which to derive a chronic REL was Prendergast *et al.* (1967). Four doses and controls were used, with 15 animals per group (45 at the lowest exposure). A NOAEL of $20 \text{ mg}/\text{m}^3$ for continuous exposure of 90 days was established. Guinea pigs showed hepatic effects (mottled livers and increased SGPT and AP enzymes) at $189 \text{ mg}/\text{m}^3$, and increased mortality at 69 to $189 \text{ mg}/\text{m}^3$. A factor of 1000 (10 for use of a subchronic study, 10 for interspecies variability, and 10 for intraspecies variability) was applied to derive the REL of $20 \mu\text{g}/\text{m}^3$. Uncertainty factors used were deemed appropriate due to the limited studies greater than 1 year in duration, lack of human epidemiological data, and toxicokinetic data. Human data does show an association between vinylidene chloride and liver toxicity.

5. Documentation Available:

CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

OEHHA, 1997a. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

OEHHA, 1997b. Chemicals known to the State to Cause Cancer or Reproductive toxicity, December, 1997. Safe Drinking and toxic Enforcement Act of 1986. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A..

Risk Assessment Advisory Committee, 1996. A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines.

Key Reference(s):

Prendergast, JA, RA Jones, LJ Jenkins and J. Siegel. 1967. Effects on experimental animals of long term inhalation of trichloroethylene, carbon tetrachloride, 1,1,1trichloroethane, dichlorodifluoromethane, and 1,1-dichloroethylene. Toxicol. Appl. Pharmacol. 10:270-289.

US EPA, 1998. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, D.C.

6. Peer Review Process and Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

The guideline is current, but California has not yet performed a data analysis for the carcinogenic risk of vinylidene chloride. Agents classified in Group C by the US EPA are not automatically considered under Proposition 65. Ten to fifteen agents are randomly picked for evaluation on a case-by-case basis.

8. Key Risk Assessment Considerations:

Oral acceptable exposure levels (mg/kg/day) have been used to calculate the inhalation reference exposure levels by assuming that a 70 kg person breaths 20 m³ per day and equal absorption occurs by the inhalation and oral routes. Vinylidene chloride is also listed as a substance whose emissions must be quantified.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses, and feedback from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.3 Agency-Specific Summary: State of Massachusetts

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* Commonwealth of Massachusetts

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL; 24-hour average) is $1.08 \mu\text{g}/\text{m}^3$ and the Allowable Ambient Limit (AAL ; annual average) is $0.02 \mu\text{g}/\text{m}^3$ corresponding to an excess lifetime cancer risk of 1×10^{-6} . The unit risk value of 5×10^{-5} per $\mu\text{g}/\text{m}^3$ is adopted from the US EPA.

4. *Application:*

"... The Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, p. ix). The Department of Environmental Protection (DEP) is responsible for developing, among other environmental programs, the air toxics program, the primary objective of which is to protect public health. The limits generated by the program are "health-based only and were developed without regard to production volume, exposure level, or regulatory implication. Similarly, economic and control technology issues are neither discussed nor considered here." (Commonwealth of Massachusetts, 1990, Volume 1, p. 4). Thus, the ambient air levels developed in this process are not to be considered as legally enforceable air standards, rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. *Documentation Available:*

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Office of Research and Standards (ORS), 1994. 1) Revisions to Massachusetts allowable ambient air limits for compounds with inhalation reference concentrations, 2) publication of updated list of Massachusetts AALs and TELs, 3) incorporation of inhalation reference concentrations into the CHEM/AAL process and 4) decisions made by ORS regarding some discrepancies observed in the RfC methodology. Letter from the ORS to the DEP, October 1994, 10 pp.

Massachusetts Department of Environmental Protection (DEP), 1995. Updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values.

Key Reference(s):

US EPA, 1985. Health Assessment Document for Vinylidene Chloride. EPA-600/8-83-031 F. EPA, ORD, OHEA, Washington, DC.

US EPA, 1998. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

International Agency for Research on Cancer (IARC), 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 19. IARC, Lyons, France.

International Agency for Research on Cancer (IARC), 1982. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. IARC Monographs, Suppl. 4. IARC, Lyons, France.

American Conference for Governmental Industrial Hygienists (ACGIH), 1986. Documentation of the Threshold Limit Values. Fifth Edition. ACGIH, Cincinnati, Ohio.

6. Peer Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the US EPA was used. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to. However, external peer reviews on the Massachusetts methodology and guideline documentation have been carried out and public input was solicited at a minimum of two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication to MOEE Staff). However, in the letter explaining the decision of the DEP to use the available US EPA's RfC values for the corresponding chemicals, no mention of public or any other type of review is mentioned.

7. Status of Guideline:

Current. The DEP estimates that each individual AAL will undergo review at least every three years. In addition, the DEP will re-issue a complete list of AALs on an annual basis in January of each year.

8. Key Risk Assessment Considerations:

Massachusetts uses occupational literature as a database for assessing acute and chronic toxicity of chemicals, and in selecting a beginning number for use in deriving preliminary human exposure limits for chemicals with threshold effects. The Most Appropriate Occupational Limit (MAOL) is defined as the occupational limit which provides the best protection against the greatest number of documented health

effects. The results of the scoring for acute and chronic health effects is obtained by combining the MAOL with a severity factor according to a scoring matrix. The weight-of-evidence classification for vinylidene chloride, for acute and toxic effects as well as animal and human carcinogenicity, places it in Group 'C' as a possible human carcinogen. Using the EPA's Gene-Tox database as the source of scientifically valid data, vinylidene chloride was given a toxicity score of 'B' for sufficient mutagenicity. For vinylidene chloride, a cumulative uncertainty factor of 18,375 was used to convert the occupational level to a TEL.

The Allowable Ambient Limit (AAL) for vinylidene chloride corresponding to an excess lifetime cancer risk of 1×10^{-6} was determined to be $0.02 \mu\text{g}/\text{m}^3$. AALs are based on both threshold and non threshold health effects and correspond to either the Threshold effects Exposure Limit (TEL) or the Non-threshold effects Exposure Limit (NTEL), whichever is lower. The NTEL for vinylidene chloride is $0.02 \mu\text{g}/\text{m}^3$ and the TEL is $1.08 \mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population. The upper bound unit cancer risk for vinylidene chloride is 5×10^{-5} . This has been adopted from the US EPA. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical is set at 1×10^{-6} . The Division of Air Quality Control plans to employ the AALs in the permitting, compliance, and enforcement components of the air toxics program.

10. Multimedia Considerations of Guidelines:

A multimedia exposure adjustment factor of 20% is systematically applied as a relative source contribution factor. The 1994 revision states that the method to derive AALs has not changed. When adequate cancer potency data exist, the approach of applying an uncertainty factor (NTEL) is used to develop a limit based on non-threshold effects. The AAL will then continue to be the lower of the values of the TEL or the NTEL (ORS, 1994).

11. Other Relevant Factors:

No information.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* Michigan (Department of Natural Resources)

3. *Guideline Value(s):*

No Initial Threshold Screening Level (ITSL) has been established for vinylidene chloride in Michigan. The Initial Risk Screening Level (IRSL), based on an annual average, is $0.02 \mu\text{g}/\text{m}^3$; the Secondary Risk Screening Level (SRSL) is $0.2 \mu\text{g}/\text{m}^3$. Vinylidene chloride is classified by weight-of-evidence as a possible human carcinogen (C) in accordance with the US EPA. The unit risk of 5×10^{-5} per $\mu\text{g}/\text{m}^3$ was calculated from a linearised multistage model.

4. *Application:*

The screening levels are developed for the implementation of Michigan's air toxics rules. These rules apply for permitting purposes. When there is emission of a toxic air contaminant, the best available control technology for toxics must be applied. Furthermore, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level.

5. *Documentation Available:*

Michigan Department of Natural Resources/ Environmental Quality, 1995/1997. Air Toxics Screening Levels. Air Quality Division.

Key Reference(s):

IRIS, 1993. US EPA Cancer Potency Value for 1,1-Dichloroethylene.

Maltoni, C. *et al.*, 1985. Experimental Research on Vinylidene Chloride Carcinogenesis. In: Archives of Research on Industrial Carcinogenesis. Vol. 3. Princeton Scientific Publishers, Princeton, NJ.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current. An updated list of screening levels that have been revised or newly established is produced every two months while a complete list of all screening levels is published at the beginning of each year.

8. *Key Risk Assessment Considerations:*

When IRSL and SRSL values are established for carcinogens, they are based on the cancer potency values published by the US EPA in the IRIS database. If these values are not available, then the EPAs HEAST

values are used as the basis. If none of these are found, then the toxicologist establishes the screening levels using inhalation toxicity data, if available.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No Information.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* New Jersey

3. *Guideline Value(s):*

There is no reference concentration (RfC) listed for inhalation. The unit risk factor for inhalation of vinylidene chloride is $5 \times 10^{-5} \mu\text{g}/\text{m}^3$ and is taken from the US EPA IRIS database. The compound is classified as a type C carcinogen according to the US EPA classification of carcinogenicity. The Air Quality Permitting Program (AQPP) assumes a linear dose-response relationship, with no threshold, for carcinogenic substances.

4. *Application:*

The list of reference concentrations for inhalation are maintained by the Department of Environmental Protection to help in developing a risk assessment for permit purposes. Risk screening, as developed by the Air Quality Permitting Program, consist of two levels. The first level risk screening uses information from permit applications and generalised worst case assumptions to estimate non-cancer and cancer risk from inhalation. Sources which fail the first level screening are submitted to a second level risk screening which uses additional information and a mathematical dispersion model to more accurately predict risk. In the case of sources which fail both screening levels, the Risk Management Committee makes its recommendation based on a case-by-case evaluation. A refined risk assessment is compulsory for certain categories of sources (coal-fired plant, medical, pathological, industrial or commercial incinerators, etc.).

5. *Documentation Available:*

New Jersey Department of Environmental Protection (NJDEP), 1994. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions, Technical manual 1003. Air Quality Permitting Program, Bureau of Air Quality Evaluation, 20 pp. + 7 Appendices.

Key Reference(s):

US EPA, 1993. Integrated Risk Information System (IRIS) Database. US Environmental Protection Agency, Washington, DC.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

Current.

8. Key Risk Assessment Considerations:

The risk screening procedure considers inhalation exposure only. Every source is not modelled individually. Instead, nomographs, developed using dispersion models, are used to calculate ambient air concentrations of each source chemical. In the case of carcinogens, the averaging time is annual, assuming ambient exposure levels to the chemical all the time. Long term effects are calculated on the basis of the maximum annual average air concentration. In the case of carcinogens, this latter concentration is multiplied by the unit risk factor to obtain the incremental risk for a chemical. In addition, New Jersey believes that just because a chemical has not shown carcinogenicity, it is not a proven non-carcinogen.

9. Key Risk Management Considerations:

Public health risk estimates of incremental risk for inhalation of carcinogens are calculated as a product of the maximum annual average ambient air concentration of a chemical ($\mu\text{g}/\text{m}^3$) and the chemical-specific unit risk factor ($\mu\text{g}/\text{m}^3$)⁻¹. The AQPP uses this information for its risk management. The policy has the following three guidelines: (1) if the incremental cancer risk is less than 1 in 10^{-6} , the risk is considered negligible, (2) if the risk is greater than 1 in 10^{-4} , the risk is considered unacceptable, and (3) if the risk lies between the preceding two values, the risk is evaluated on a case-by-case basis.

10. Multimedia Considerations of Guidelines:

The risk screening procedure considers only exposure by the inhalation route.

11. Other Relevant Factors:

No information.

11.6 Agency-Specific Summary: State of New York

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* New York State Department of Environmental Conservation

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC; 1-h average air concentration) is 2,000 $\mu\text{g}/\text{m}^3$ and the Annual-average-based Guideline Concentration (AGC) is 0.02 $\mu\text{g}/\text{m}^3$. Vinylidene chloride is classified as a high toxicity air contaminant and is given an "A" 6NYCRR Part 212 Environmental Rating. For compounds with such a rating, the maximum annual average ambient impact is required not to exceed the AGC. Similarly, the one hour short-term SGC must also not be exceeded. "A" rated compounds also require the application of "Best Available Control Technology" (BACT) to achieve 99% or greater pollution control.

4. *Application:*

"... The guidelines ... are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212, 257." (NY DEC, 1991, p. 1). These guidelines are not established as ambient air quality standards but they are intended to protect the general public from adverse effects that may be induced by exposure to ambient air contaminants. These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. The guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. *Documentation Available:*

New York State Department of Environmental Conservation (DEC), 1991. New York Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation., Albany, New York NY, 20 p. + Appendices.

Key Reference(s):

United States Environmental Protection Agency (US EPA), 1986. Guidelines for Carcinogen Risk Assessment. Federal Register 51: 33992-34003. (9/24/86)

American Conference of Governmental Industrial Hygienists (ACGIH), 1990-1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, Ohio.

6. *Peer Review Process and Public Consultation:*

The scientific documents prepared by the New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guidelines development process.

7. Status of Guideline:

Current. The New York State Air Guide - 1 is dated 1991. The latest version of the companion Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

8. Key Risk Assessment Considerations:

Vinylidene chloride is classified as a high toxicity air contaminant by New York State (1994). This classification includes human carcinogens, potential human carcinogens and other substances posing a significant risk to humans. Classification is based on data from epidemiology studies, the full range of toxicology studies in animals, and a review of the scientific and medical literature. Data from inhalation studies takes precedence over data from studies using other routes of exposure. Particular attention is paid to information on carcinogenic or genotoxic potential. Models using low-dose linearity are preferred unless there is sufficient evidence to support another dose-response extrapolation model. The derivation of the AGC is based on studies with data that show biologically and statistically significant tumour type incidence, duration and route of exposure, as well as, the greatest sensitivity. In the absence of appropriate scientific data, the dose extrapolation from animal to human is performed by surface area conversion. The ACGIH (TLV-STEL) of 79,000 $\mu\text{g}/\text{m}^3$ was divided by 4.2 to extrapolate to continuous exposures and 10 for toxicity class to derive its Short-Term Guideline Concentration (SGC) of 2,000 $\mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

Environmental Ratings are reviewed for each contaminant every time a Certificate to Operate comes up for renewal. A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses to be employed in the permitting process.

10. Multimedia Considerations of Guidelines:

Considers human airborne exposure only.

11. Other Relevant Factors:

No information.

11.7 Agency-Specific Summary: World Health Organisation (WHO)

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* World Health Organisation

3. *Guideline Value(s):*

No information.

4. *Application:*

The WHO Air Quality Guidelines are intended to provide a basis to protect public health from adverse effects of air pollution, and to provide background information and guidance to governments in making risk management decisions. However, it should be noted that no standards as such are promulgated by the WHO.

5. *Documentation Available:*

WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organisation, Regional Office for Europe, Copenhagen, Denmark, 426p.

Key Reference(s):

None.

6. *Peer Review Process and Public Consultation:*

Scientific background documents were prepared by experts and submitted to working groups consisting of international experts to provide a basis for discussion. After a series of meetings and internal and external reviews by experts and representatives of the Member States of the Region, the resultant conclusions and recommendations were presented at a final meeting where they were adopted by consensus of the representatives. In addition, peer-reviewed scientific research data were employed in the development of these documents.

7. *Status of Guideline:*

Current. Vinylidene chloride is still under investigation.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No information.

10. *Multimedia Considerations of Guidelines:*

No information.

11. *Other Relevant Factors:*

No information.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* The Netherlands Ministry of Housing, Spatial Planning and the Environment

3. *Guideline Value(s):*

No national air limit value or target value has been specified for vinylidene chloride. The emission standard is $20,000 \mu\text{g}/\text{m}_3$ for a mass flow of 0.1 kg per hour or more. Vinylidene chloride is classified as gO.1, an organic substance in gaseous or vapour form.

4. *Application:*

Limit values are non-statutory environmental quality objectives that are considered policy guidelines. They should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effect-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effect-oriented guidelines.

The target value is the level at which the risk of adverse effects to the ecosystem, functional properties of the environment or other compartments are considered negligible. The ultimate objective of the environmental quality guidelines of The Netherlands is that the target value might eventually become similar to the limit value.

5. *Documentation Available:*

Netherlands MHSPE, 1994. Environmental Quality Objectives in The Netherlands. A review of environmental quality objectives and their policy framework in The Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 pp.

NeR Staff Office, 1992. The Netherlands Emission Regulations - Air. Netherlands Emission Regulation Staff Office, Bilthoven, The Netherlands. 81 pp. + Appendices.

Van de Plassche, E.J. and G.J.M. Bockting, 1993. Towards Integrated Environmental Quality Objectives for Several Volatile compounds. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. Report no. 679101 011.

Key Reference(s):

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances, but are only available in Dutch.

6. Peer Review Process and Public Consultation:

No specific information on this issue was presented in the available English documentation.

7. Status of Guideline:

Current. Vinylidene chloride is still under review.

8. Key Risk Assessment Considerations:

No information.

9. Key Risk Management Considerations:

Risk management is carried out by progressive criteria setting. In principle, the target value is set to either the negligible concentration or the naturally occurring background value, whichever is higher. A limit value should not be exceeded and a guidance value should be avoided whenever possible. With time, the values are tightened to reach the target value.

10. Multimedia Considerations of Guidelines:

Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. Information is currently available on the MPC and the NC (negligible concentration) of water, soil, sediment and air.

11. Other Relevant Factors:

No information.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. Name of Chemical: Vinylidene chloride

2. Agency: Swedish Environmental Protection Agency

3. Guideline Value(s):

No guidelines.

4. Application:

No information.

5. Documentation Available:

Victorin, K., 1993. Health effects of urban air pollutants: guideline values and conditions in Sweden. *Chemosphere* 27: 1691-1706.

Victorin, K., 1997. Personal communication.

Key Reference(s):

None.

6. Peer Review Process and Public Consultation:

No information.

7. Status of Guideline:

No information.

8. Key Risk Assessment Considerations:

No information.

9. Key Risk Management Considerations:

No information.

10. Multimedia Considerations of Guidelines:

No information.

11. Other Relevant Factors:

No information.

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Vinylidene chloride

2. *Agency:* Environment Canada

3. *Guideline Value(s):*

No information.

4. *Application:*

No information.

5. *Documentation Available:*

Canadian Environmental Protection Act (CEPA), 1993-94. CEPA Priority Substance List (PSL-1)-
Assessment Reports (Environment and Health Canada).

Key Reference(s):

Vinylidene chloride was not considered under PSL-1. It will also not be considered under PSL-2.

6. *Peer Review Process and Public Consultation:*

No information.

7. *Status of Guideline:*

No information.

8. *Key Risk Assessment Considerations:*

No information.

9. *Key Risk Management Considerations:*

No Information.

10. *Multimedia Considerations of Guidelines:*

No Information.

11. *Other Relevant Factors:*

No information.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level (Massachusetts)</i>
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration (New York State)</i>
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
µg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram

MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or Ontario Ministry of Environment and Energy
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences</i> (USA)
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program</i> (USA)
OEHHA	<i>Office of Environmental Health Hazard Assessment</i> (California EPA)
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level'</i> as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or <i>'Recommended Exposure Limit'</i> used by both NIOSH and ATSDR
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumorigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumorigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>

**RATIONALE FOR THE DEVELOPMENT OF
ONTARIO AIR STANDARDS
FOR
XYLENE**

February 2000

**Standards Development Branch
Ontario Ministry of the Environment**

 **Ontario**

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999, identified candidate substances for the development of air standards for the next several years. Xylene (a mixture of *ortho*-, *para*- and *meta*-isomers) was identified as a priority for review based on both its pattern of use in Ontario, and recent toxicological information published since the existing standard was originally developed in 1969 and was re-affirmed in 1985. A review of scientific and technical information relevant to setting air quality standards for xylene has previously been provided to stakeholders for their comment. This document provides the rationale for recommending an Ambient Air Quality Criterion (AAQC) and a half-hour Point of Impingement (POI) standard for xylene.

Xylene mostly exists as a mixture of *ortho*, *meta* and *para* isomers. Commercial xylene typically consists of 20% *ortho*-xylene, 40% *meta*-xylene and 20% *para*-xylene, with 15% ethylbenzene and smaller amounts of other aromatic hydrocarbons. A range of odour threshold values have been reported for xylene from 0.35 to 174 mg/m³.

Xylene has a wide range of industrial uses. It is used as an octane enhancer in gasolines and fuel manufacturing, as a solvent in paint formulations, inks, dyes, adhesives, cleaning and degreasing agents, and it is also used in paint removers. Xylene is also contained in pesticide formulations as well as being used extensively as a solvent in research laboratories and as feedstock for toluic acids. The individual isomers also have specific industrial applications.

The 1997 National Pollutant Release Inventory (NPRI) lists 126 sources with atmospheric releases of xylene in Ontario totalling 4,876 tonnes. Releases to other environmental media are minor, with atmospheric releases accounting for greater than 99 % of the total. Levels of xylene (*m*- and *p*-isomers) in ambient air in Ontario range from below the detection limit to a maximum of 179 µg/m³ (24-hour average), with a mean concentration of 3.6 µg/m³. Half-hour maximum concentrations measured near point sources ranged as high as 160 to 200 µg/m³.

Occupational exposure studies and studies with volunteers indicated that short-term inhalation exposure (15-minutes) to xylene (2,000 mg/m³) can cause irritation to the eyes, nose, and throat. Xylene is considered a central nervous system (CNS) depressant, and exposure to concentrations between 390 to 870 mg/m³ for 8-hour periods was sufficient to produce effects such as delayed reaction time and impaired manual coordination and balance. Epidemiological studies suggest that chronic occupational exposure to 14 ppm (58 mg/m³; 8-hour average, geometric mean) can increase symptoms such as headaches, eye and nasal irritation, and a floating sensation. Data on the developmental and reproductive toxicity of xylene are inconclusive. Some animal studies suggest that exposure to levels

greater than 1,000 mg/m³ during gestation can retard fetal growth and cause skeletal abnormalities. Xylene does not appear to be mutagenic and is not considered a possible human carcinogen by the United States Environmental Protection Agency (US EPA) and the International Agency for Research on Cancer (IARC).

Ontario currently has a 24-hour AAQC and a half-hour POI standard for xylene of 2,300 µg/m³. These criteria have been established on the basis of odour and health effects.

In revising the air quality standards for Ontario, the Ministry of the Environment is reviewing and considering risk assessments, standards, and guidelines used by environmental agencies world-wide. This report reviews the scientific basis for air quality guidelines and standards developed by the US EPA, the States of California, New York, New Jersey, Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government.

Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific rationale which support the acute and chronic inhalation Reference Exposure Levels of 2,200 µg/m³ and 300 µg/m³, respectively, of the State of California, and the tolerable concentration of the Environment Canada and Health Canada. However, the chronic REL of the State of California is considered a more appropriate basis for the derivation of a health-based AAQC because the REL was obtained from reliable human studies and effects on the central nervous system are considered the most sensitive endpoint for the adverse effects of xylene. Therefore, the current California chronic REL of 300 µg/m³ has been employed as the basis to derive Ontario's health-based 24 hour AAQC of 1,500 µg/m³, using a dispersion modelling method. The odour nuisance is considered a sensitive factor based on the odour thresholds of xylene. Therefore, the current odour-based POI standards of 2,300 µg/m³ is maintained.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and considering other relevant information such as the aesthetic effects (i.e., odour nuisance) of xylene, the Ministry is proposing the following Ambient Air Quality Criterion and Point of Impingement standard for xylene:

- a 24-hour average AAQC of 1,500 µg/m³ (micrograms per cubic metre of air) for xylene based on the adverse health effects of this compound; and,
- a half-hour POI standard of 2,300 µg/m³ (micrograms per cubic metre of air) for xylene based on the odour nuisance and the adverse health effects of this compound.

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1.0 Introduction

Ontario regulates air emissions in order to achieve and maintain air quality which is protective of human health and the environment. The *Environmental Protection Act* (Section 9) requires that all stationary sources that emit, or have the potential to emit, a contaminant obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

The Ministry of the Environment uses a combination of regulated point of impingement (POI) standards and point of impingement guidelines in reviewing Certificates of Approval (MOEE, 1994a), each of which is derived by mathematical scaling, from an ambient air quality criterion (AAQC). Ambient Air Quality Criterion (AAQCs) represent human health or environmental effect-based values, and are normally set at a level not expected to cause adverse effects based on continuous exposure. As such, economic factors, such as technical feasibility and costs, are not explicitly considered when establishing AAQCs.

Point of impingement standards are scheduled in Regulation 346 and can be used directly as enforcement tools. The regulation (Section 5(3)) specifies that a source cannot, "cause or permit the concentration of a contaminant at a point of impingement to exceed the standard prescribed in Schedule 1". All sources are required to comply with the standards in Regulation 346 unless they are specifically exempt. The concentration of a contaminant at a POI may be calculated in accordance with the Appendix of Regulation 346 (Air Dispersion Models). Since POI standards specified under Regulation 346 apply to all sources, economic issues need to be taken into account in their development to ensure that the standards are technically feasible, and that both the benefits and costs of improved ambient air quality are assessed.

In addition to POI standards established under Regulation 346, the Ministry also has a large number of POI guidelines. These are used by the Ministry to assess general air quality, and the *potential* for causing adverse effect (MOEE, 1994a). Like the POI standards specified in Regulation 346, POI guidelines are used in reviewing applications for Certificates of Approval, to approve new and modified emission sources. Once incorporated into a legal instrument such as a Certificate of Approval, POI guidelines are legally binding. However, unlike POI standards in Regulation 346, they do not automatically apply to existing sources at the time they are approved.

In assessing the available information for a substance, when the Ministry believes that meeting the proposed standard immediately will not be possible due to implementation issues related to economics, technical feasibility and the time needed to establish appropriate control technology, the Ministry will propose a range of values within which an interim standard will be set. This range of values is based on the following considerations:

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- For carcinogens, the interim standard will be set within a range of air concentrations which corresponds to a risk level of 1 excess cancer in a population of 1,000,000 (10^{-6}) over a lifetime up to, but no higher than, 1 excess cancer in a population of 10,000 (10^{-4}) over a lifetime and;
 - For non-carcinogens, the range under consideration for the interim standard is from the proposed POI standard up to 10 times this proposed standard. In cases where the reduction in the standard for a non-carcinogen is less than 10-fold overall, the upper end of the range for the interim standard is selected at a value which at least 90% of facilities in Ontario are anticipated to be able to presently meet based on MOE's records of emissions and modelled ground level concentrations.

The interim standard which is ultimately selected will be considered a first step in a ramping down process to a final standard. The final POI standard will be the lower number of the range from which the interim standard is selected. The ramping down characteristics, including an appropriate timeframe, will be discussed with stakeholders as part of the detailed risk management phase which will be undertaken by the Ministry subsequent to this posting. An interim standard will constitute the POI standard in force until such time it is revised through the risk management process.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in October, 1999 (MOEE, 1996; MOE, 1999), identified 70 high priority substances for which current air standards will be reviewed, over the next several years. Factors used by the Ministry to determine which contaminants require priority include potential degree of exposure, volume of use, toxicity, Federal/Provincial commitments and sensitive sub-populations, including children. All high priority substances will be standards (as opposed to guidelines) and will be in Schedule 1 of Regulation 346. In March 1998, following the 1996 initiative, the Ministry proposed a multi-step process for developing air quality standards (MOE, 1998). As an initial step, risk assessment and risk management information, relevant to establishing a standard for a particular compound, was documented and made available for stakeholder review. This provided stakeholders with the opportunity to critically review the information and provide any additional information they felt should be considered by the Ministry in setting an air quality standard for a particular compound.

Xylene was identified as a priority for review based on its pattern of use in Ontario and toxicological information published since the existing standards were established. This report reviews scientific and technical information relevant to setting an AAQC and a POI standard for xylene.

2.0 General Information

2.1 Physical/Chemical Properties

The following list provides some general information on xylene (representing a mixture of *o*-, *m*-, and *p*-isomers, unless otherwise stated):

CAS #	1330-20-7
RTECS #	ZE2100000
UN #	1307
Conversion Factors	1 ppm = 4.35 mg/m ³ @ 25 °C 1 mg/m ³ = 0.23 ppm @ 25 °C
Boiling Point	138.5 °C
Flash Point	37.8 °C
Henry's Law Constant	5.19×10^{-3} to 7.70×10^{-3} atm m ³ /mol @ 25 °C
Log K _{ow}	3.12 to 3.20
Formula	C ₆ H ₄ (CH ₃) ₂
Molecular Weight	106.16 g/mol
Vapour Density (air = 1)	3.7
Vapour Pressure	5 to 6.5 mm @ 20 °C, 6.62 to 8.78 mm @ 25 °C
Common Synonyms	Dimethylbenzene, Methyltoluene, and Xylol

Xylene is a clear, colourless, flammable liquid which has an aromatic, hydrocarbon-like odour. It has a range of odour threshold values from 0.35 to 174 mg/m³ (ACGIH, 1991; Environment Canada and Health Canada, 1993a). AIHA (1989) reports a geometric mean of 5.4, 0.62 and 2.1 ppm (or 23, 2.7 and 9 mg/m³), for the *ortho*, *meta*, and *para* isomers, respectively. Commercial grade xylene consists of a mixture of *ortho*-, *para*-, and *meta*-isomers, the proportion of each being dependent on the source. Xylene derived from petroleum sources contains approximately 20% *o*-, 44% *m*-, and 20% *p*-xylene, and 15% ethylbenzene, whereas coal tar derived xylene consists of about 10-15% *o*-, 45-70% *m*-, and 28% *p*-xylene, and 6-10% ethylbenzene (Environment Canada and Health Canada, 1993a).

2.2 Uses of Xylene

Xylene is used as octane enhancers in gasolines and fuel manufacturing, as solvents in inks, dyes, adhesives, cleaning and degreasing agents, and in paint removers (Environment Canada and Health Canada, 1993a). Xylene is also contained in pesticide formulations, as well as being used extensively

as solvents in medical research, educational laboratories and as feedstock for the manufacture of toluic acids. The individual isomers also have specific industrial applications (Environment Canada and Health Canada, 1993a). The most industrially important isomer is *p*-xylene, most of which is oxidized to terephthalic acid and dimethyl terephthalate. This is the first step in producing poly(ethylene terephthalate) for use in fibres, films and resins. *o*-Xylene is primarily used in the manufacture of phthalic anhydride, used to make plasticizers in vinyl plastics. *m*-Xylene is required in the manufacturing of isophthalic acid, which is used as the base of unsaturated polyester resins acid, as well as isophthalonitrile, which is used for the production of the fungicide tetrachloroisophthalo-nitrile (Environment Canada and Health Canada, 1993a).

2.3 Sources and Levels

Xylene is a solvent widely used in a number of industrial and commercial applications. The 1997 National Pollutants Release Inventory (NPRI) reports a total of 7,268 tonnes of xylene released in Canada. There were 126 sources of xylene in Ontario, which released a total of 4,876 tonnes to the atmosphere (NPRI, 1997). Releases to other environmental media are minor, with atmospheric releases accounting for greater than 99% of the total. The majority of these releases originate from painting operations associated with motor vehicle manufacturing, as well as from the manufacturing of plastic and rubber mouldings.

Environment Canada has collected ambient air data for xylene from January 1993 to December 1995 from thirty-nine monitoring stations across Canada (Environment Canada, 1997). From 4,230 samples tested for — and *p*-xylene, a mean concentration of $3.64 \pm 4.85 \mu\text{g}/\text{m}^3$ was observed (Environment Canada, 1997). The concentrations reported ranged from no detection (Detection Limit of $0.1 \mu\text{g}/\text{m}^3$) to $179.65 \mu\text{g}/\text{m}^3$ (Environment Canada, 1997). From 4,231 samples tested for *o*-xylene, a mean concentration of $1.32 \pm 1.61 \mu\text{g}/\text{m}^3$ was observed (Environment Canada, 1997). The concentrations reported ranged from no detection (detection limit of $0.1 \mu\text{g}/\text{m}^3$) to a maximum of $57.53 \mu\text{g}/\text{m}^3$ (Environment Canada, 1997).

Half-hour average concentrations of xylene in Ontario were monitored by the MOEE. Xylene was detected in a range of 0.04 to $200 \mu\text{g}/\text{m}^3$ (MOEE, 1997). The highest levels were detected in the vicinity of chemical waste facilities in Elmira and Samia at concentrations of $200 \mu\text{g}/\text{m}^3$ and $29 \mu\text{g}/\text{m}^3$, respectively, and in the vicinity of an Asphalt plant in Vineland at a concentration of $160 \mu\text{g}/\text{m}^3$ (MOEE, 1997). In 1989, the mean concentration of mixed xylenes recorded at the rural site of Walpole Island, Ontario was $2.2 \mu\text{g}/\text{m}^3$ (24-hour average) and the highest combined mean concentration at any one Ontario urban site was $25.9 \mu\text{g}/\text{m}^3$ (Environment Canada and Health Canada, 1993a).

From an analysis of applications for Certificates of Approval from 1988 to 1997 in Ontario, a sample of over 500 sources were identified, with emissions of xylene covered by a Certificate. These

certificates cover a wide range of industrial operations including automotive manufacturing, furniture manufacturing, and plastics and allied products. The largest component of these Certificates cover emissions from painting operations and paint spray booths. The median Ground Level Concentration (maximum half-hour average) predicted by Regulation 346 dispersion modelling, for a sampling of 250 sources, is approximately $81 \mu\text{g}/\text{m}^3$, with eight of the sources having GLCs above $1000 \mu\text{g}/\text{m}^3$.

2.4 Environmental Fate

The major atmospheric removal process for xylene is phototransformation with hydroxy radicals, resulting in the production of formic and acetic acids. Xylene reacts slowly with ozone and is not associated with the destruction of the stratospheric ozone layer. Xylene is a member of a class of volatile organic chemicals (VOCs) that react with oxides of nitrogen in the presence of sunlight to form ground-level ozone, a component of smog. Xylene does not contribute to global warming (CEPA, 1993). Volatilization and microbial degradation are the major removal mechanisms for xylene present in water. Environment Canada and Health Canada (CEPA, 1993) conclude that xylene is not expected to persist or bioaccumulate in the environment.

3.0 Toxicology of Xylene

The following toxicological review of xylene primarily focusses on inhalation, which is the predominant route of human exposure. Data on other exposure routes are included where relevant or where inhalation data are lacking.

Studies showed that pulmonary uptake of mixed xylenes in the lungs was 60 - 65% (reviewed in Environment Canada and Health Canada, 1993a and ATSDR, 1995). The extent of pulmonary absorption was shown to be independent of the level and duration of exposure. Xylene is also readily absorbed from the gastrointestinal tract after ingestion of the compound. Dermal absorption of xylene is poor and likely accounts for only a very small fraction of the total exposure to xylene for the general public (Environment Canada and Health Canada, 1993a).

Once absorbed in the blood, all xylene isomers are rapidly distributed to several different areas of the body. Xylene is very soluble in fat tissue, and as a result, relatively high concentrations of xylene can be isolated in subcutaneous adipose tissue. Xylene also sequesters in the kidneys, liver, lungs, blood, muscles, spleen and brain, and reach maximum tissue concentrations within 1-2 hours following absorption. Xylene is generally metabolized by cytochrome P-450 to methylbenzoic and methylhippuric acids. This is accomplished via the oxidation of the methyl groups and the subsequent conjugation or hydroxylation of the parent compound and/or metabolites. Xylene is primarily excreted in urine in the form of these metabolites, with only 5% of their total excretion in the form of the parent

compound. Elimination of xylene is rapid, and complete excretion is achieved within 18-20 hours of cessation of exposure (reviewed in Environment Canada and Health Canada, 1993a and ATSDR, 1995).

There appears to be no substantial difference between the toxicity of different isomers of xylene (ACGIH, 1991). A review of human and animal studies suggest that xylene mixtures, *m*-xylene, *p*-xylene and *o*-xylene produce similar effects, although there may be some variability in the relative potency of the individual isomers (ATSDR, 1995).

3.1 Acute Toxicity

Xylene vapour is irritating to the eyes, nose and throat at levels above 200 ppm (870 mg/m³) (reviewed in Calabrese and Kenyon, 1991; HSDB, 1994). Irritation was reported in several human volunteers exposed to mixed xylene vapours at concentrations equal to or greater than 1,000 mg/m³ for 15 minutes. Volunteers exposed to 1,300 mg/m³ xylene for 70 minutes experienced slight and transient impairment of some central nervous system functions during exercise. Effects from exposure may include headaches, nausea, ataxia, vomiting, anorexia, short-term memory loss, incoordination, disorientation, congestion, pulmonary edema and irritation of the respiratory system (reviewed in Environment Canada and Health Canada, 1993a; HSDB, 1994). The American Conference of Governmental Industrial Hygienists (ACGIH) reports a 4-hour LC₅₀ of 3,900 ppm (17,000 mg/m³) for xylene in rats (ACGIH, 1991).

3.2 Subchronic and Chronic Toxicity

A limited number of studies have investigated the subchronic toxicity associated with inhalation exposure to xylene (ACGIH, 1991). Chronic inhalation exposure to either individual or mixed xylene produces irritation of the eyes and the respiratory system, headaches, disorientation, ataxia and other effects on the central nervous system. In a study of about 300 workers, 175 of whom were occupationally exposed to mixed xylenes for an average of 7 years, no changes were observed in haematology and serum biochemistry over non-exposed control populations (Uchida *et al.*, 1993). The authors concluded that mixed xylenes are not toxic to hematopoietic (blood forming) organs or the liver. However there was an exposure-related increase in the incidence of specific symptoms such as headaches, eye and nasal irritation and light headedness (floating sensation). Estimated exposure levels were about 14 ppm or 58.4 mg/m³ (Geometric mean of an 8-hour average concentration).

Among the limited 90-day continuous exposure animal studies available, the lowest concentration at which an increase in liver to body weight ratio was observed was 1,400 mg/m³ in rats. This transient effect was seen following 30 days of exposure, but not following 90 days of exposure (reviewed in Environment Canada and Health Canada, 1993a). The effects of exposure up to 810 ppm (3,500

mg/m³) for 6 hours/day, 5 days/week, for 13 weeks, in rats and dogs have been investigated. No adverse effects were reported in either rats or dogs within this concentration range (reviewed in ACGIH, 1991, Environment Canada and Health Canada, 1993a).

In a one-year inhalation study, male CFY rats exposed to 4,750 mg/m³ *o*-xylene for 8 hours/day, 7 days/week exhibited liver toxicity, altered enzyme patterns, and increased bromosulphophthalein retention time (indicative of decreased clearance). Proliferation of the smooth endoplasmic reticulum, increased numbers of peroxisomes and autophagous bodies, glycogen depletion, and occasionally damaged mitochondria were revealed by histological examination (Tatrai *et al.*, 1981 as cited in Calabrese and Kenyon, 1991).

3.3 Developmental and Reproductive Toxicity

Data on the developmental and reproductive toxicity of xylene are inconclusive. Some inhalation studies have shown that xylene is not teratogenic, but induce fetotoxicity at levels below which any maternal toxicity is evident (reviewed in ACGIH, 1991; Calabrese and Kenyon, 1991; Environment Canada and Health Canada, 1993a; ATSDR, 1995). Foetotoxic effects include skeletal variations, delayed bone development, decreased fetal weights and altered enzyme activity in both rats and mice. For *p*-xylene, a LOAEL for foetotoxicity and maternal toxicity of 150 mg/m³ has been suggested (Ungvary, *et al.*, 1980 as cited in Calabrese and Kenyon, 1991). In a compilation of embryotoxic effects of xylene and other aromatic solvents on mice, rats and rabbits, Ungvary and Tatrai report unspecified maternal toxicity at 250 mg/m³ (57.5 ppm) with delayed skeletal development in foetuses when exposed continuously at days 7-15 of gestation (Ungvary and Tatrai, 1985).

In a more recent study involving rats exposed to 200 ppm (870 mg/m³) xylene mixture for 6 hours/day on days 4-20 of pregnancy, the only effect noted in newborns was impaired performance of females in a test designed to assess motor ability (Hass and Jakobsen, 1993). The differences were not large and did not appear to persist.

3.4 Genotoxicity and Carcinogenicity

Assays measuring the mutant reversion in several strains of *Salmonella typhimurium* or *Escherichia coli*, the frequency of recessive lethal mutation in *Drosophila*, and those assays investigating chromosomal damage in bone marrow cells of rats exposed to xylene by inhalation, all reported negative findings (Calabrese and Kenyon, 1991; Environment Canada and Health Canada, 1993a; US EPA, 1994). Studies investigating the frequency of sister chromatid exchange and chromosomal aberrations in human lymphocytes exposed to xylene gave no evidence of mutagenic activity (US EPA, 1994).

The US EPA has classified xylene in Group D (not classifiable as to human carcinogenicity). Orally administered technical grade xylene mixtures did not cause significant increases in tumour incidence in rats or mice of either gender (US EPA, 1994). The International Agency for Research on Cancer (IARC) has classified xylene as Group 3 carcinogenic compounds, i.e., not classifiable as to their carcinogenicity (IARC, 1996).

3.5 Environmental Effects

The Priority Substances List Assessment (PSL) of xylene concluded that there is insufficient information to assess the exposure of wildlife in the aquatic environment or the potential effects to birds (Environment Canada and Health Canada, 1993b). However, the PSL assessment determined that xylene is unlikely to have adverse effects on birds or aquatic animals.

Significant leaf injury to barley plants was noted after a 4-hour exposure to xylene (Currier, 1951). Studies of the exposure of runner beans (*Phaseolus multiflorus*) and parsnips (*Pastinaca sativa*) to xylene for one hour resulted in a relatively small difference between the concentrations that did not damage the plants and those that killed the plant leaves, making it difficult to determine EC₅₀ values. For o-xylene, the concentration range between "no-effect" and leaf death was 19,575 mg/m³ to 29,145 mg/m³ (4,500 - 6,700 ppm) and for p-xylene, it was 24,360 mg/m³ to 40,020 mg/m³ (5,600 - 9,200 ppm) (ECETOX, 1986).

Leopard frog (*Rana pipiens*) larvae were exposed to m-xylene and a 96-hour LC₅₀ of 3.5 mg/L was determined (Black et al, 1982). Aquatic toxicity data for freshwater fish indicate that 96-hour LC₅₀ values range from 6.7 mg/L for rainbow trout (*Salmo gairdneri*) to 35 mg/L for guppies (*Poecilia reticulata*) (ECETOX, 1986). The water flea, *Daphnia magna*, is particularly sensitive to xylene, demonstrating a 24-hour LC₅₀ values of 1 mg/L to 4.7 mg/L (Environment Canada and Health Canada, 1993b).

4.0 Existing Ambient Air Quality Criteria

4.1 Overview

Ontario currently has a half-hour POI standard and a 24-hour AAQC for xylene of $2,300 \mu\text{g}/\text{m}^3$. Both values were established on the basis of odour and health effects of this compound (MOEE, 1994a).

The documentation for ten agencies, including the United States Federal Government, the States of California, New York, New Jersey and Michigan, the Commonwealth of Massachusetts, the World Health Organization, The Netherlands, the Swedish Institute of Environmental Medicine and the Canadian Federal Government, was reviewed for the existence and basis of air quality criteria for xylene. A summary of air quality guidelines and standards used in other jurisdictions is provided in Table 1. Reviews of specific agencies are provided in section 11.0 of the Appendix.

In reviewing the air quality guidelines and exposure limits presented in Table 1, it should be noted that the Ministry of the Environment normally uses a factor of 15 to convert from criteria based on annual average concentrations, to half-hour POI standards, and a factor of 3 to convert from criteria based on 24-hour average concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). However, depending on the health end-point being considered, other conversion factors may also be employed.

Of the ten agencies reviewed, only the US EPA and the World Health Organization do not have a current inhalation guideline for xylene. The US EPA withdrew its reference concentration (RfC) of $300 \mu\text{g}/\text{m}^3$ for xylene pending further review. For the other agencies, several, as a matter of policy, have adopted the Threshold Limit Value-Time Weighted Average (TLV-TWA) of 100 ppm ($435 \text{ mg}/\text{m}^3$) established by the American Council of Governmental Industrial Hygienists (ACGIH). These agencies include California (acute), Massachusetts (acute and chronic), Michigan (acute), and New York (acute). The U.S. state agencies apply a variety of factors to the TLV in order to extrapolate from occupational exposures to environmental exposures protective of the general population. Guidelines based on the TLV range from a low of $11.80 \mu\text{g}/\text{m}^3$ (Massachusetts; 24-hour and annual average) to a high of $100,000 \mu\text{g}/\text{m}^3$ (New York; 1-hour average).

Michigan's initial Threshold Screening Level ($4,400 \mu\text{g}/\text{m}^3$; 1-hour average) is based on consideration of short-term irritation effects. On the basis of independent reviews, New Jersey and Health Canada have established lifetime average daily exposure values of $165 \mu\text{g}/\text{m}^3$ and $180 \mu\text{g}/\text{m}^3$, respectively. Both New Jersey's Reference Concentration (RfC) and Health Canada's Tolerable Concentration (TC) are based on considerations of reproductive and developmental effects resulting from chronic exposure. Though the US EPA has withdrawn their Reference Concentration of $300 \mu\text{g}/\text{m}^3$ pending further

review, New York State has chosen to maintain the RfC as the basis for its annual guideline, until such time the US EPA establishes a new value.

It is noted that both the acute Reference Exposure Level (REL) and chronic REL of California are undergoing public review. California is proposing to revise its acute REL from 4,400 $\mu\text{g}/\text{m}^3$ to 2,200 $\mu\text{g}/\text{m}^3$, and the chronic REL from 300 $\mu\text{g}/\text{m}^3$ to 700 $\mu\text{g}/\text{m}^3$ (OEHHA, 1998; OEHHA, 1999). The proposed chronic REL is based on occupational exposures in which exposed subjects reported symptoms such as eye and nasal irritation, headaches and light-headedness (OEHHA, 1999). The proposed acute REL is based on an occupational study which reported no effects from short-term (3-minute) exposure to 100 ppm xylene and noticeable eye and throat irritation at 200 ppm (OEHHA, 1998).

Table 1. Summary of Existing Air Quality Guidelines⁽¹⁾ for Xylene

Agency	Guideline Value	Basis of Guideline	Date ^a	Comments
US EPA (IRIS)	No ambient air exposure limits are available.			
	RfC (Reference Concentration)		1998	Under Review
California	Chronic REL: 300 $\mu\text{g}/\text{m}^3$; proposed, 700 $\mu\text{g}/\text{m}^3$ (annual average) Acute REL: 4,400 $\mu\text{g}/\text{m}^3$; proposed, 2,200 $\mu\text{g}/\text{m}^3$ (1-hour average)	Health Effects Assessment Summary Tables (HEAST) from US EPA. TLV-TWA from ACGIH.	1993	Proposed chronic and acute RELs are undergoing public review
Massachusetts	TEL (Threshold Effects Exposure Limits): 11.80 $\mu\text{g}/\text{m}^3$ (24-hour average).	TLV-TWA from ACGIH.	1995	Adjusted to allow for exposures via other media.
	AAL (Allowable Ambient Limit): 11.80 $\mu\text{g}/\text{m}^3$ (annual average).	TLV-TWA from ACGIH.	1995	
Michigan	ITSL (Initial Threshold Screening Level): 4,400 $\mu\text{g}/\text{m}^3$ (1-hour average).	Studies of CNS and reproductive effects in humans.	1997	Permitting standard, i.e., the Predicted Ambient Impact of a toxic from any facility cannot exceed its screening level.
New Jersey	RfC: 165 $\mu\text{g}/\text{m}^3$ (24-hour average).	Reference Air Level (RAL) from Northeast States for Coordinated Air Use Management (NESAUM).	1994	Permitting application. The RfC must be used to assess cancer risks in the risk assessments conducted as part of a permit application.
New York State	SGC (Short-term Guideline Concentration): 100,000 $\mu\text{g}/\text{m}^3$ (1-hour average).	TLV-TWA from ACGIH.	1991	Used for permitting.
	AGC (Annual Guideline Concentration): 300 $\mu\text{g}/\text{m}^3$.	RfC from US EPA.	1991	Used for permitting.
WHO	None.		1987	
Netherlands	100,000 $\mu\text{g}/\text{m}^3$ (half-hour average).	Emission standard.	1997	Used for permitting.
	National MIC (Maximum Immissible Concentration): 240 $\mu\text{g}/\text{m}^3$ (annual average).	Province of Groningen's guideline.		Target value: to be identified.
Sweden	None for xylene only. 40.5-405 $\mu\text{g}/\text{m}^3$ (long-term average) for a sum of toluene and xylene.	Health-based.	1993	Supporting documentation was only available in Swedish.
CEPA	TC (Tolerable Concentration): 180 $\mu\text{g}/\text{m}^3$ (24-hour average for a lifetime)	Study of fetal and maternal effects in rats.	1996	provisional based on limitations of primary study

Ontario	half-hour POI standard: 2,300 $\mu\text{g}/\text{m}^3$. 24-hour AAQC: 2,300 $\mu\text{g}/\text{m}^3$.	Both the POI and AAQC are based on odour.	1985	
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1. Includes guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
2. Refers to when the health-based guideline background report or the original legislative initiative was issued. For the US EPA, date refers to when the latest review of the RFC was conducted, if applicable, or the date the IRIS database was accessed.

4.2 Evaluation of Existing Criteria

In setting air quality standards and recommended exposure limits for xylene, all agencies examined have treated xylene as a mixture because of the similar toxicological profiles of the three isomers. Several agencies have established limits based on an extrapolation from the occupational Threshold Limit Value of 100 ppm (435 mg/m^3), established by the ACGIH. This value is based on the avoidance of odour or irritation effects of xylene in the workplace. Depending on the policies of the individual jurisdictions, agencies may apply different safety factors resulting in a considerable range of potential guidelines.

Allowable exposure limits and air quality guidelines developed by other agencies are based on one of three approaches: extrapolation from the occupational Threshold Limit Value (TLV), which is based on the avoidance of irritation effects in the workplace; extrapolation from animal studies using developmental effects as the end-point; or extrapolation from occupational studies. The states of Michigan and New Jersey have established exposure limits for xylene based on a critical review of the primary and secondary literature.

The Tolerable Concentration (TC) of 180 $\mu\text{g}/\text{m}^3$ set by Health Canada is based on a study by Ungvary and Tatrai (1985). This study examined the embryotoxic effects of xylene and other alkyl derivatives of benzene in mice, rats and rabbits. Rats were exposed on days 7 to 15 of gestation, for 24 hours per day, to a xylene mixture (unspecified composition) at concentrations ranging from 0 (control group) to 3400 mg/m^3 . At 250 mg/m^3 (the lowest administered concentration), approximately 32% of day-21 fetuses displayed some form of delayed skeletal development compared to 13% in the unexposed control group. There was no apparent dose-dependency in the effect noted however, the same percentage of fetuses displayed deficits in all three exposure groups (250 mg/m^3 , 1900 mg/m^3 and 340 mg/m^3). The authors also reported that the xylene mixture caused moderate maternal toxicity which was dose-dependent, although details on the types of effects were not provided (Ungvary and Tatrai, 1985). On the basis of this study, Health Canada determined 250 mg/m^3 to be the lowest-observed-effects-level (LOEL) for meaningful effects in the most sensitive species. The LOEL was then adjusted by a factor of 1,000. This value was the result of the combined uncertainly factors of, 10 to account for interspecies extrapolation [rats to humans], 10 to account for intraspecies variation, and 10 for

extrapolating from a LOEL to a no-observed-effects-level (NOEL) and the "limitations" of the critical study. The LOEL was also adjusted to account for differences in the ratio of the inhalation volume/body weight of rats [(0.11 m³/day)/0.35 kg] to humans aged 5 to 11 years [(12 m³/day)/27 kg]. These adjustments resulted in a provisional Tolerable Concentration (TC) of 0.18 mg/m³. The TC is defined as the airborne concentration to which a person can be exposed continuously over a lifetime without deleterious effect (Health Canada, 1996a).

The study of Ungvary and Tatrai has a number of limitations which make it difficult to critically evaluate. These limitations include: the authors do not specify the composition of xylene used; results are expressed in terms of total animals rather than litters; and details are lacking with respect to the methods used and results obtained (Ungvary and Tatrai, 1985). Health Canada acknowledges these limitations by rating the TC as provisional (Health Canada, 1996b).

Subsequent to the assessment by Health Canada under CEPA, Hass and Jackobsen (1993), presented results on the effects of xylene on the teratogenicity and postnatal development of rats. Animals were exposed via inhalation to 0 or 200 ppm (870 mg/m³) mixed technical grade xylene for six hours per day, on days 4 - 20 of gestation. One group of litters was examined for teratogenic effects on day 21, while another was taken to term and examined post-natally. The teratology study revealed that 18 of 26 litters in the exposed group displayed delayed ossification of specific bones in the skull which was evident in only 2 of 22 litters in the unexposed control group. However, the authors pointed out that this observation was difficult to interpret since it was not accompanied by any other evidence of delayed ossification or altered skeletal development (Hass and Jackobsen, 1993).

Based on the study of Hass and Jackobsen (1993), the Agency for Toxic Substances and Disease Registry (ATSDR) of the United States Department of Health Services established a Minimal Risk Level (MRL) for intermediate duration exposures (15-364 days) of 0.7 ppm (2.8 mg/m³) (ATSDR, 1995). For the offspring of rats exposed to 200 ppm (870 mg/m³) there was a slight impairment in the performance on a Rotarod performance test (a behavioural test for motor ability). At this level of exposure, no maternal toxicity was noted, but it is not clear if this was a permanent or transient effect. The 200 ppm is considered a LOAEL. The MRL of 0.7 ppm is derived by dividing the LOAEL of 200 ppm by a total uncertainty factor of 300.

The State of California is proposing to revise its REL for xylene to 700 µg/m³ from 300 µg/m³, based on a study involving workers exposed to xylene in a plant manufacturing rubber boots and plastic coated wire and for printing operations for an average of 7 years (OEHHA, 1999). Estimates of exposure to xylene were made by using diffusion samplers for individual monitoring of 994 workers during a single eight-hour shift. Of these, 175 (107 men and 68 women) were selected for further study based on the fact that xylene accounted for at least 70% of their occupational exposure to solvents. The geometric mean of xylene concentrations for the exposed workers was approximately 14.2 ppm

(58 mg/m³). The control group consisted of 241 (116 men and 125 women) unexposed workers from the same factories or factories from other regions with matching age distribution, time in this occupation, incidence of alcohol consumption and cigarette usage. Health examinations comparing haematology, serum biochemistry and subjective symptoms were conducted for the exposed and a matched control population (Uchida et al., 1993).

Results of the survey indicated that exposures to xylene induced central nervous system effects and effects of local irritation to the eyes, nose and throat. A significant ($p < 0.01$) increase in five subjective symptoms such as, dimmed vision, dizziness, unusual taste, and heavy feeling in the head and headache in either men or women experienced during work was reported. The frequency of four symptoms such as eye irritation, nasal irritation, sore throat and floating sensation in both men and women was significantly ($p < 0.01$) elevated. Three of these subjective symptoms such as irritation in the eyes, sore throat and floating sensation appeared to show dose-dependency. Evaluation of haematological parameters and serum biochemistry did not reveal any significant changes between the exposed and unexposed groups. However, a significant ($p < 0.01$) increase in the frequency of an elevated ratio of alkaline phosphatase to leucine aminopeptidase and aspartate aminotransferase to alanine transferase may indicate changes in liver functions (Uchida et al., 1993).

From this study, California assessed the geometric mean of exposure of 14.2 ppm (58 mg/m³) as the Lowest Observed Adverse Effects Level (LOAEL). This was adjusted for continuous exposure giving a human equivalent LOAEL of 5.1 ppm (22.2 mg/m³). A total uncertainty factor of 30 was applied (3 to account for uncertainty in relating the LOAEL to a NOAEL, and 10 to account for intraspecies variability) to the adjusted LOAEL to derive a chronic inhalation REL of 161 ppb or 700 µg/m³ (OEHHA, 1999). Also based on this study, ATSDR set a chronic minimum risk level (MRL) at hazardous waste sites of 0.1 ppm or 434 µg/m³ (ATSDR, 1995).

The strength of the reference exposure level is that it was derived from a human study involving long-term exposure to xylene (average duration of 7 years of work). The neurological effects considered were a sensitive endpoint and this view was supported by a number of human and animal inhalation studies (ATSDR, 1995). Exposure was characterized by both personal monitors and urinary metabolite analysis, and workers were examined for clinical signs, haematology, serum biochemistry and subjective symptoms. The main weakness is that exposure was monitored for only one shift, which provided a time-weighted 8-hour average concentration. Certain symptoms such as eye irritation, sore throat and floating sensation could be the result of peak exposures higher than the geometric mean of 14.2 ppm (58 mg/m³).

5.0 Responses of Stakeholders to the Information Draft

In January 1999, the Ministry posted information draft documents for eighteen chemicals, including xylene, for air quality standards development under the Standards Plan (MOEE, 1996; MOE 1999). The Ministry requested input regarding: the completeness of relevant inhalation toxicological information examined by the Ministry and the rationale of the agencies that the Ministry has considered appropriate for the development of air quality standards. Particularly, the chronic inhalation REL and its rationale proposed by the State of California, and technical and economic impacts that may be anticipated consequent to the revision of the air quality standards.

During the consultation period, the Ministry received four submissions from stakeholders regarding the draft document for xylene. Comments from the petroleum products stakeholders indicated that a full risk management process would be required if a significant reduction from the current standard was intended. The automotive manufacturing stakeholders supported the scientific rationale from California EPA's proposed chronic REL, but disagreed with the uncertainty factor employed to derive this criterion and further stated that any reduction of the POI standard from its current level would induce significant technical and economic impacts. In addition, one automotive equipment and parts industry stakeholder suggested that the chronic REL was a reasonable basis; however, possible economic and technical impacts should be considered if the current air quality standards were lowered. Comments from a utility industry stakeholder suggested that the facility would have no problem meeting a lower standard.

6.0 Overview of the next Phase of the Ministry's Standards Setting Process

The comments from stakeholders for the first phase of the standards development process (information drafts) for this substance were evaluated and utilized in formulating the recommendations which appear later in this document. This first phase, which represented the opportunity for stakeholders to comment on the toxicological and other scientific information used in the development of the air quality standard is now complete. During the initial phase stakeholders were also encouraged to provide information on technical and/or economic considerations or concerns.

The Ministry is now soliciting comments from stakeholders regarding the proposed AAQC and POI standard which are presented in Section 8.0 below. This is the next phase in the overall process of standards development. The goal of this phase is to arrive at a decision regarding the determination of air quality standards for xylene.

7.0 Considerations in the Development of Air Quality Standards for Xylene

The existing 24-hour AAQC and POI standard for xylene in Ontario are both set at $2,300 \mu\text{g}/\text{m}^3$. These criteria are based on the odour nuisance and health effects of xylene as limiting effects.

Xylene is widely used in industrial solvents. The main route of exposure to the general public is through air. Reports based on human studies suggest that both short- and long-term exposures to xylene result in various adverse effects to the central nervous system. Other effects include irritation to the eyes, nose and throat. Like many organic solvents, prolonged exposure can result in narcotic effects, dizziness, headaches, mental confusion, and tremors. The liver and kidneys may also be target organs for xylene toxicity. Animal studies suggest that the developing foetus may be sensitive to exposure to xylene and this effect constitutes the rationale supporting the provisional Tolerable Concentration of $180 \mu\text{g}/\text{m}^3$ of Environment Canada and Health Canada. A study of workers from a rubber boots manufacturing, plastic coated wire, and printing operations factory who were exposed to an average concentration of 14.2 ppm ($58 \text{ mg}/\text{m}^3$) xylene for seven years found no indication of adverse impact on liver, kidney, or haematological functions. Some of the workers indicated subjective symptoms such as eye irritation, sore throat, floating sensation and reduced appetite. Based on this study, California is proposing a chronic inhalation REL of $700 \mu\text{g}/\text{m}^3$ and this criterion is currently under public review.

Reported odour detection threshold values range from 0.30 to $174 \text{ mg}/\text{m}^3$ (AIHA, 1989). The AIHA reports a geometric mean of $2,700 \mu\text{g}/\text{m}^3$ for the odour threshold for *m*-xylene, the lowest geometric mean odour threshold of the three isomers. This odour threshold value is similar to the acute REL of $2,200 \mu\text{g}/\text{m}^3$ (one-hour average) proposed by the State of California.

8.0 Recommendations

The Ministry of the Environment has reviewed and considered air quality guidelines and standards used by leading agencies world-wide. Of the criteria reviewed from other agencies, the Ministry has evaluated and accepted the scientific rationale which supports the acute and chronic inhalation REL of $2,200 \mu\text{g}/\text{m}^3$ and $300 \mu\text{g}/\text{m}^3$, respectively, of the State of California, and the Tolerable Concentration of $180 \mu\text{g}/\text{m}^3$ of the Environment Canada and Health Canada. However, the REL of the State of California should be considered the more appropriate basis for the derivation of a health-based AAQC because the REL was obtained from reliable human studies and effects on the central nervous system are considered the most sensitive endpoints for the adverse effects of xylene. Therefore, the current California chronic REL of $300 \mu\text{g}/\text{m}^3$ is employed as the basis to derive Ontario's health-based 24 hour AAQC.

The Ministry of the Environment uses a factor of 5 to convert from criteria based on annual average concentrations to 24-hour average concentrations and a factor of 15 to convert from criteria based on annual average concentrations to half-hour POI concentrations. These factors are derived from empirical measurements and are selected to ensure that if the short-term limit is met, air quality standards based on longer-term exposures will not be exceeded (MOE, 1987; MOEE, 1994b). Thus, a 24-hour AAQC of $1,500 \mu\text{g}/\text{m}^3$ can be obtained from the REL of $300 \mu\text{g}/\text{m}^3$. A half-hour health-based POI limit of $4,500 \mu\text{g}/\text{m}^3$ could be derived from the REL of $300 \mu\text{g}/\text{m}^3$. However, the odour nuisance is considered a sensitive factor based on the odour thresholds of xylene. Therefore, the current odour-based POI standards of $2,300 \mu\text{g}/\text{m}^3$ is maintained.

In summary, based on the information reviewed from leading agencies, the assessment of toxicological information, and considering other relevant information such as the aesthetic effects (i.e., odour nuisance) of xylene, the Ministry is proposing the following Ambient Air Quality Criterion and Point of Impingement standard for xylene:

- a 24-hour average AAQC of $1,500 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for xylene based on the adverse health effects of this compound; and,
- a half-hour POI standard of $2,300 \mu\text{g}/\text{m}^3$ (micrograms per cubic metre of air) for xylene based on the odour nuisance and the adverse health effects of this compound.

9.0 A Guide for Stakeholders Responding to this Posting

The Ministry welcomes comments on this proposal from all interested parties. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the above recommendations. It is also important that submissions from stakeholders include the rationale and reasoning supporting their stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments. The information provided in the submissions will undergo a preliminary risk management analysis within the Ministry in order to determine whether there are compelling implementation issues associated with the standard. If there are, it is likely that a more detailed risk management process will be needed. In the absence of specific, significant implementation issues the Ministry will proceed to finalize the proposed standards.

In order to demonstrate significant implementation issues such as economic impacts and/or technical difficulties in meeting the proposed standard, in the near term, a submission from a company subject to the standard should include the following information:

1. The operations or processes which give rise to emissions of the substance(s) under review;

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2. The reduction in emissions that would be required to bring the facility into compliance with the proposed standard;
 3. Changes in equipment, potential additional systems or operations (including pollution prevention measures) necessary to achieve and maintain compliance with the proposed standard; including
 - projected capital and annual operating costs of such changes
 - timing
 - any gains in productivity, recovered materials or reduced energy or raw material usage
 4. If it is claimed that a standard is not technically achievable, provide documentation of the conditions or circumstances that confirms this position.
 5. Provide documentation as to the degree of reduction in emission and ground-level concentration that could be achieved in the operation, facility and/or firm, where compliance with the proposed standard is considered.

In addition, where it is determined that a proposed standard cannot be achieved immediately, please indicate the earliest possible time frame for compliance with the standard.

During discussion with stakeholders regarding air quality standards, the matter of dispersion models used to estimate air quality concentrations at point of impingement has been raised. Currently, O. Reg. 346 states that: "The concentration of a contaminant at a point of impingement *may* be calculated in accordance with the Appendix" Section 5(2). The Appendix to Reg 346 outlines three air dispersion models that may be used depending on the site-specific circumstances. Although in the majority of cases the Ministry uses the existing Reg 346 models, there have been instances where other models, such as USEPA's Industrial Source Complex (ISC3), have been used on a site-specific basis.

The Ministry intends to undertake future discussion on the introduction of newer models into policy and regulation, including the United States Environmental Protection Agency's (USEPA) ISC suite of models and the proposed AERMOD model. The introduction of new models will likely influence all other Ministry air quality standards and guidelines as well as the substance addressed in this posting. To this end, the Ministry acknowledges that, if stakeholders make their comments on this substance based on the current use of the air dispersion models, any changes in the models may lead to changes in stakeholders opinions and comments.

The Ministry also appreciates that responding firms may be committed to, or involved in, developing emission reduction strategies under the federal Strategic Options Processes. Please advise the Ministry, in your submission, whether you are a participant in a Strategic Options Process with the federal government that could result in reductions in the use and/or release of this substance from your operations, facility and/or firm. If so, please identify how these anticipated emission reductions, will affect predicted Ground Level Concentrations from your facilities under the existing model.

The foregoing is provided as guidance on the type of information that would assist the Ministry in its ongoing analysis and decision-making in setting an air standard for this substance. In some cases, where it is not feasible to provide all of the information noted within the comment period, the Ministry would appreciate the respondent addressing as many of the issues as possible to ensure an informed decision is made. If stakeholders make no comments about the proposed standards, it will be presumed that they have no concerns or will have no difficulty, technically or financially, in complying with the proposed standard.

In addition to the general guidance above, the following Ministry documents provide more detail regarding the type of information that would be considered by the Ministry in its standard setting process:

- The Guidance document, *"Procedure for Preparing an Emission Summary and Dispersion Modelling Report - June 1998"* may assist you in completing the air emissions compliance assessment with the proposed air standard;
- MOE Guideline F-14 (formerly 02-01), *"Economic Analyses of Control Documents on Private Sector Enterprises and Municipal Projects"* Economic Services Branch- April 1994, and;
- *"Framework for the Application of Socio-economic Analyses in Setting Environmental Standards."* Economic Integration Task Group, Canadian Council of Ministers of the Environment, 1998.
<http://www.mbnet.mb.ca/ccme/pdfs/SEFrameENG.pdf>

Comments relevant to the setting of air quality standards for xylene can be sent to:

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NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

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OEHHA, 1999. Air toxics Hot Spots Program Risk Assessment Guidelines: Part III, Technical Support Documentation for the Determination of Non Cancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

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State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

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11.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

11.1 Agency-Specific Summary: Federal Government of the United States

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* United States Environmental Protection Agency (US EPA)

3. *Guideline Value(s):*

The Reference Concentration (RfC) for exposure to xylenes is not currently available. A risk assessment for xylenes is under review by an Agency work group. Xylene mixtures have a human carcinogenic classification of "D", i.e., not classifiable as to human carcinogenicity. No air concentration guideline exists for xylenes.

4. *Application:*

The US EPA has prepared and maintained a database of health risk and regulatory information. This database is called the Integrated Risk Information System (IRIS) and was developed to provide consistent risk information on chemical substances for use in decision-making and regulatory activities. The values reported in IRIS do not represent guidelines or standards.

5. *Documentation Available:*

US EPA, 1998. Integrated Risk Information System (IRIS) Computerised Database. United States Environmental Protection Agency, Washington DC.

6. *Peer-Review Process and Public Consultation:*

The US EPA makes use of peer-reviewed scientific literature to assess the hazard and to evaluate the potential dose-response relationship of the chemical under review. The assessment methodology and the chemical-specific information undergo scientific and policy reviews.

7. *Status of Guideline:*

Current.

8. *Key Risk Assessment Considerations:*

Not applicable.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No adjustment for multimedia exposure is considered in the development exposure concentrations for threshold effects or unit risk values for non-threshold effects.

11. *Other Relevant Factors:*

None.

11.2 Agency-Specific Summary: State of California

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* State of California Office of Environmental Health Hazard Assessment (OEHHA); California EPA, Air Resources Board (ARB); California Air Pollution Control Officers Association (CAPCOA)

3. *Guideline Value(s):*

The State of California does not identify any specific air quality guideline value for xylenes. However, a risk-based chronic reference exposure level (REL) of $300 \mu\text{g}/\text{m}^3$ (annual average) has been adopted for the sum of the three isomers of xylene, based on the United States Environmental Protection Agency's (US EPA) Health Effects Assessment Summary Table (HEAST). California has recently proposed revising the chronic REL to $700 \mu\text{g}/\text{m}^3$ (OEHHA, 1999).

The State of California has also established an acute one-hour REL of $4,400 \mu\text{g}/\text{m}^3$ for the sum of the three isomers of xylene. This REL is currently being revised by the State and a new acute one-hour REL of $2,200 \mu\text{g}/\text{m}^3$ is being proposed and released for public comment (ARB, 1997a).

4. *Application:*

The Revised 1992 Risk Assessment Guidelines were developed by CAPCOA to provide guidance for the risk assessment procedures which are to be used for the Air Toxics "Hot Spots" Program. This program is based on the California State law *Air Toxics "Hot Spots" Information and Assessment Act* detailed under the Health and Safety Code, Section 44360 *et seq.*, 1987. This Act requires local Air Pollution Control Districts to identify facilities in their area which will conduct health risk assessments, outline how such assessments should be prepared and detail how the results are to be used in prioritizing substances for needs assessments. These guidelines were prepared to provide a methodology by which consistent risk assessments will be performed, thereby facilitating the comparison and review of such reports. The State does not consider these exposure levels to be legally enforceable air quality guidelines or limit values as they should not be employed outside the scope of the program.

The Toxic Air Contaminant Identification List was compiled by the OEHHA and the ARB as part of the State's Air Toxic Program Assembly Bill (AB)-1807. This draft report presents individual summaries detailing the general exposure and health effects for the 244 substances identified on this list. The summaries are not based upon new California EPA evaluations and do not revise California EPA judgements or policies about the potential for these pollutants to cause harm to human health. Though

this document identifies risk-based guidance values which have been established or accepted by the OEHHA, the original documentation for such values should be consulted in order to review the conditions under which these values should be reviewed, interpreted and applied.

5. Documentation Available:

ARB, 1996. Toxic Air Contaminant Identification List - Summaries (Draft Report). California Environmental Protection Agency - Air Resources Board. Pages 969-972.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

OEHHA, 1999. Air toxics Hot Spots Program Risk Assessment Guidelines: Part III, Technical Support Documentation for the Determination of Non Cancer Chronic Reference Exposure Levels. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, California, U.S.A.

6. Peer-review Process and Public Consultation:

The Draft Toxic Air Contaminant Identification list is currently undergoing an extensive peer-review and is open for public review and comments. The sources which were used to compile the technical summaries for the 244 substances identified on the Toxic Air Contaminants Identification List were taken from existing governmental exposure and health effects databases (eg., HSDB, IRIS, etc.) and additional widely recognised reference texts.

The reference concentrations, RELs and cancer potency values reported in both the Draft Toxic Air Contaminant Identification List and the CAPCOA documents were prepared and/or adopted for consideration by the OEHHA after extensive review. The rationales for the derivation of all of these values have undergone public review and consultation. Any risk assessment conducted under these guidelines are subjected to review by the local district and the OEHHA. In addition, public input plays a key role in the identification and prioritisation of the areas and facilities for which risk assessments are required.

7. Status of Guideline:

Not applicable.

8. Key Risk Assessment Considerations:

The chronic REL of 300 $\mu\text{g}/\text{m}^3$ was adopted from a Reference Concentration (RfC) listed in the 1991 HEAST tables. This RfC was subsequently withdrawn by the EPA and is currently under review. OEHHA acknowledges that the chronic REL for xylenes, as reported under the CAPCOA guidelines, is out of date. OEHHA has re-evaluated their chronic REL for xylene and is recommending to revise

to 700 $\mu\text{g}/\text{m}^3$ from the current value of 300 $\mu\text{g}/\text{m}^3$. The proposed value is based on the expression of subjective symptoms in workers chronically exposed to mixed Xylenes (OEHHA, 1999).

The acute REL of 4,400 $\mu\text{g}/\text{m}^3$ was adopted from the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value-Time Weighted Average (TLV-TWA) of 434,000 $\mu\text{g}/\text{m}^3$, modified by an uncertainty factor of 100 and rounded upwards. The OEHHA considered this TLV to be the lowest-observed-adverse-effects level (LOAEL) for acute exposure in humans (CAPCOA, 1993). The toxicological endpoint considered in the development of the acute REL was respiratory irritation (ARB, 1996). The proposed new acute one-hour REL of 2,200 $\mu\text{g}/\text{m}^3$ is derived from an epidemiological study which investigated the effects of xylenes on the respiratory system (ARB, 1997a). This study reported a no-observed-adverse-effects level (NOAEL) of 100 ppm following a 3-minute exposure interval (ARB, 1997a). Noticeable eye, nose and throat irritation was observed following a 3-minute exposure to 200 ppm (ARB, 1997a). The proposed new REL was calculated by adjusting this NOAEL by a factor of 10, to account for intraspecies variability, and extrapolating from a 3 minute to a one-hour exposure (ARB, 1997a).

Proposition 65 Safe Drinking Water and Toxic Enforcement Act was issued in 1986 by the California Environmental Protection Agency. This Act details the current status of daily intake levels which have been derived or adopted for carcinogens and reproductive toxicants identified by the OEHHA (ARB, 1996). California has not set a daily intake value for xylenes. The State recognises that the US EPA's RfC is currently under review (ARB, 1996). Xylenes are not listed under Proposition 65 as a reproductive or developmental toxicant, nor as a carcinogen (ARB, 1996).

Xylenes are identified on the June 1996 Toxic Air Contaminants Identification List but has yet to undergo a "needs assessment" which is the State's next step in establishing a potential air quality guideline value (ARB, 1997b).

9. Key Risk Management Considerations:

Not applicable

10. Multimedia Considerations of Guidelines:

The State of California requires risk assessments to consider exposure to certain substances via non-inhalation pathways (specific compounds are listed under Table III-5 in CAPCOA, 1993). Xylenes are not among these substances.

11. Other Relevant Factors:

Xylenes are identified by CAPCOA as a quantifiable and reportable substance in any risk assessment undertaken by a facility posting emissions and/or any risk assessment which is required under the "Hot Spots" Program. Annual average and maximum one hour concentrations of xylenes must also be

measured, calculated and/or reported by the State, as well as any facility posting emissions in order to be used in the analysis of cancer risk and/or chronic non-cancer effects.

11.3 Agency-Specific Summary: Commonwealth of Massachusetts

1. *Name of Chemical:* Xylenes (CAS# 1330-20-7)

2. *Agency:* Commonwealth of Massachusetts, Department of Environmental Protection (MDEP)

3. *Guideline Value(s):*

The Threshold Effects Exposure Limit (TEL) for the sum of the three isomers of xylene is $11.80 \mu\text{g}/\text{m}^3$ (24-hour average). The TEL is based on consideration of threshold effects. The Allowable Ambient Limit (AAL) for the sum of the three isomers of xylene is $11.80 \mu\text{g}/\text{m}^3$ (annual average). The AAL is based on consideration of threshold and non-threshold effects.

4. *Application:*

The TEL and AAL guidelines are to be employed in the permitting, compliance and enforcement of the Commonwealth of Massachusetts air quality program. The primary goal of the TELs and AALs developed by MDEP is to protect public health from any air contaminant causing known or potentially deleterious effects. These guidelines were developed without regard to production volume, exposure level, regulatory implication, economic considerations, or control technology issues.

5. *Documentation Available:*

MDEP, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits. Vol. I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts. May 1990.

MDEP, 1994. Memorandum from the Office of Research and Standards dated October 20, 1994. This memorandum outlines a number of revisions to the 1990 Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Air Limits, Commonwealth of Massachusetts, Department of Environmental Protection, Boston, Massachusetts.

MDEP, 1995. Summary Table of Massachusetts Threshold Effects Exposure Limits (TELs) and Allowable Ambient Limits (AALs) for Ambient Air. Massachusetts Department of Environmental Protection (MDEP), Office of Research and Standards, Boston, Massachusetts. December 1995.

Key Reference(s):

ACGIH, 1988. Threshold Limit Values and Biological Indices 1987-1988. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

6. *Peer-Review Process and Public Consultation:*

In the development of the Massachusetts ambient air guidelines, peer-reviewed scientific data and analyses from both public and government sources were used. Toxicological information and exposure limits from the following agencies were reviewed: United States Environmental Protection Agency (US EPA), the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP), the National Institute of Occupational Safety and Health (NIOSH), the American Conference of Governmental Industrial Hygienists (ACGIH), and the Occupational Safety and Health Administration (OSHA). Internal and external peer-review and public consultation processes have been carried out since 1982.

7. *Status of Guideline(s):*

Current. Guidelines may be updated periodically.

8. *Key Risk Assessment Considerations:*

The MDEP has developed a policy for establishing air limits. The methodology addresses both threshold and non-threshold effects, with the selection of the final AAL based on the most sensitive effect. The process focuses primarily on hazard identification and dose-response assessment.

Threshold Effects

Assuming that a chemical has a threshold for an adverse effect(s), occupational limits are used to derive the TEL. Where a reference concentration (RfC) exists for a chemical and is published in the Integrated Risk Information System (IRIS) by the US EPA, the methodology outlined in MDEP (1990) has been adapted (MDEP, 1994) to include the RfC in the derivation of TELs and AALs where appropriate and defensible. In the case of xylenes, no IRIS RfC was reported. The MDEP, after having reviewed the ACGIH Threshold Limit Value - Time Weighted Average (TLV-TWA) occupational exposure limit for xylenes, has adopted the level of 433.8 mg/m³ for use in the MDEP air guidelines. This level was considered the Most Appropriate Occupational Limit (MAOL) and was adjusted by the following factors:

- I. divided by 4.2 to account for continuous exposure. This adjusts the occupational exposure limit which considers exposure to occur for 8 hours per day, 5 days per week, to consider continuous exposure.
- II. divided by 1.75 to account for differences in sensitivity between adults and children.
- III. divided by 10 to account for high-risk groups and other sensitive sub-populations.
- IV. divided by 10 to account for incomplete data in the toxicity database used to review the potential toxicity of xylene.

The factor applied to the MAOL to calculate the "adjusted" MAOL is, therefore, 735. The adjusted MAOL is numerically equivalent to 0.59020 mg/m³ (590.20 µg/m³). At this point, another set of

uncertainty factors were applied to the adjusted MAOL:

- I. divided by 10. The Threshold Effects Uncertainty Factor (TEUF) is an uncertainty factor which accounts for acute, chronic, developmental or reproductive effects that may not have been considered in the health risk assessment of the occupational limit. The MDEP applied a TEUF of 10 for xylenes.
- II. divided by 5 to account for exposure through media other than air. This is based on an assumption that ambient air contributes only 20% of the total exposure.

The total uncertainty factor applied to adjust the ACGIH occupational exposure limit is 36,750. The TEL was, therefore, calculated as $11.8 \mu\text{g}/\text{m}^3$.

Non-Threshold Effects

The MDEP reported that there was inadequate evidence to classify xylenes' mutagenic potential. There was no positive evidence to classify xylenes' carcinogenic potential and a positive result for xylenes structure activity relationship (SAR) analysis (MDEP, 1990). The MDEP scores SAR as "positive" if a substance or its metabolites falls into Group C of the United States Food and Drug Administration's (USFDA) 1982 *Toxicological Principles for the Safety Assessment of Direct Food Additive and Color Additives Used in Food* (MDEP, 1990). The Non-Threshold Effect Exposure Limit (NTEL) was developed from the adjusted MAOL ($590.2 \mu\text{g}/\text{m}^3$) using a Non-Threshold Effects Uncertainty Factor (NTEUF) of 5 to account for the positive SAR analysis. No adjustment was made for multimedia considerations. The resulting NTEL for xylenes was calculated as $118.04 \mu\text{g}/\text{m}^3$.

Allowable Ambient Limit

The AAL is the lower of the TEL or NTEL. Therefore, the TEL for xylenes was adopted as the AAL. The xylenes AAL is $11.8 \mu\text{g}/\text{m}^3$.

9. Key Risk Management Considerations:

The selection of the AAL is based on the most sensitive end point of an adverse health effect. The goal of the process is the protection of human health. For carcinogens, the AAL derived in the MDEP process corresponds to a maximum allowable excess lifetime cancer risk of one in one million (10^{-6}) or less. The process of derivation of air guidelines does not consider technological, economic or enforcement issues.

10. Multimedia Considerations of Guidelines:

A factor of 20% was applied to the adjusted MAOL used as the basis of the TEL guideline to allow for contributions from exposure media other than air. However, the AAL does not consider other sources of exposure.

11. *Other Relevant Factors:*

None.

11.4 Agency-Specific Summary: State of Michigan

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* State of Michigan Department of Environmental Quality (DEQ)

3. *Guideline Value(s):* The Initial Threshold Screening Level (ITSL) for the sum of the three isomers of xylene is 4,400 mg/m³, with an averaging time of 1 hour.

4. *Application:*

Screening levels are used for the implementation of Michigan's Air Toxic Rules (Rules 230-232), which apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant (State of Michigan, 1995). There are two basic requirements of the air toxic rules as follows:

- i) each source must apply the best available control technology for toxics (T-BACT);
- ii) after the application of T-BACT, the Predicted Ambient Impact (PAI) of each toxic air contaminant cannot exceed its screening level.

The PAI of each toxic air contaminant is determined using the maximum hourly emission rate for that substance from the facility applying for a permit. The PAI is determined by application of a dispersion model or screening method in accordance with specific regulatory provisions (set out in R336.1240 or R336.1241, or both), by a screening method using a Dilution Matrix included in R336.1230 (Table 22), or by a screening method approved by the regulatory authority.

Screening levels for each toxic air contaminant are developed by the Air Quality Division (AQD) of the DEQ and are applied across the state. They are used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The intent is to protect ambient air, but the screening levels are not ambient air standards *per se*. Rather, they are health-based levels which the PAI of emissions from a subject facility cannot exceed. If the PAI exceeds the screening level set for a substance, facility-specific physical or operational changes will be required to reduce emissions in order for a permit to be issued.

5. *Documentation Available:*

State of Michigan, 1989. Final Report of the Michigan Air Toxics Policy Committee-A Proposed Strategy for Processing Air Quality Permit Applications for New Emission Sources of Toxic Air Pollutants. Michigan Department of Natural Resources.

State of Michigan, 1992. R336.1230 Air Toxics from new and modified sources.

State of Michigan, 1993. Recommendations of the Scientific Advisory Panel-Xylene. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1995. Procedures for Developing Screening Levels. Michigan Department of Natural Resources, Air Quality Division.

State of Michigan, 1997. List of Screening Levels (ITSL, IRS�, and SRS�) for Michigan's Air Toxic Rules. Michigan Department of Environmental Quality, Air Quality Division.

Key Reference(s):

Biodynamics, 1982. Parental and fetal reproduction toxicity study. Submitted to the EPA by API, document #FYI-AX-0983-0209.

Carpenter, C.P., E.R. Kinkead, D.L. Geary, L. Sullivan, and J.M. King, 1975. Petroleum hydrocarbon toxicity studies. V. animal and human response to vapours of mixed xylenes. *Toxicol. Appl. Pharmacol.* 33:543-558.

Gamberale F., G. Arnwall, and M. Hultengren, 1978. Exposure to xylene and ethyl benzene. III. Effects on central nervous system functions. *Scand. J. Work Environ. Health* 6:94-103.

Hake *et al.*, 1981. P-Xylene: development of a biological standard for the industrial worker by breath analysis. PB82-152844.

Rosengren, L.E., P. Kjellstrand, A. Aurell, and K.G. Haglid, 1986. Irreversible effects of xylene on the brain after long-term exposure: a quantitative study of DNA and the glial cell marker proteins S-100 and FGA. *Neurotoxicology* 7:121-133.

Savolainen and Seppalainen, 1979. Biochemical and physiological effects of organic solvents on rat axon membranes isolated by a new technique. *Neurotoxicology* 1:467-477.

6. Peer-Review Process and Public Consultation:

Peer-reviewed scientific research data, analyses and evaluations from various sources were employed in the development of the ITSL.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The health assessment methodology used by the DEQ for non-carcinogenic compounds involves

determination of an ITSL. The ITSL is a regulatory level used in evaluating the acceptability of emissions from new and modified sources of toxic air pollutants. The ITSL is set at some fraction of the observable threshold dose determined in studies using laboratory animals or from humans. The methodology for determining the ITSL is contained in Rule 232.

The ITSL for xylenes was adopted by the AQD following a review and recommendation by the Scientific Advisory Panel (SAP) (State of Michigan, 1993). The Advisory Panel's recommendation of 1 ppm (4,400 $\mu\text{g}/\text{m}^3$) for xylenes included consideration of animal data for both central nervous system (CNS) effects (neurochemical changes) and possible reproductive effects (mating performance). The SAP of the AQD concluded that human occupational experience and limited clinical studies suggest some individuals may complain of minor eye irritation at exposures of 100 ppm and above, and transient effects on CNS function may occur at approximately 300 ppm and above.

Following their review of the scientific literature, the SAP agreed upon a 1 ppm exposure limit based upon the animal and human data, without distinguishing between the severity of the effects observed in different studies. They further concluded that this value reflects the "weight-of-evidence" in regard to establishing a single long-term exposure limit for xylenes which incorporated an appropriate margin of uncertainty for each of the studies considered and which would be protective against all possible effects. No specific information is provided regarding the mathematical derivation of the ITSL.

9. Key Risk Management Considerations:

None.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.5 Agency-Specific Summary: State of New Jersey

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* State of New Jersey Department of Environmental Protection (NJDEP)

3. *Guideline Value(s):*

The State of New Jersey has not set an air quality standard for xylenes (NJDEP, 1997a). The State has proclaimed a reference concentration (RfC) of 165 $\mu\text{g}/\text{m}^3$ for the sum of the three xylene isomers.

4. *Application:*

The NJDEP Air Quality Permitting Program (AQPP) requires risks to be assessed in conjunction with applying for an air pollution control pre-construction permit. Risks are assessed either by a risk screening conducted by AQPP staff or by a refined risk assessment completed by the applicant. The approach chosen is based on the type and size of the facility or source. The risk assessment must address any toxic air contaminant declared under the New Jersey Administrative Code Toxic Substances List (7:27-17) or which are listed on the Federal Hazardous Air Pollutants List posted under the *Clean Air Act* (NJDEP, 1994b).

5. *Documentation Available:*

NJDEP, 1994a. Technical Manual 1003 - Air Quality Regulation Program Bureau of Air Quality Evaluation: Guidance on Preparing Risk Assessment for Air Contaminant Emissions. New Jersey Department of Environmental Protection, Air Quality Permitting Program, Bureau of Air Quality Evaluation.

NJDEP, 1994b. New Jersey Administrative Code Title 7, Chapter 27, Subchapter 17 - Control and Prohibition of Air Pollution by Toxic Substances.

Key Reference(s):

NESCAUM, 1989. Evaluation of the Health Effects from Exposure to Gasoline and Gasoline Vapours - Final Report Executive Summary. Northeast States for Coordinated Air Use Management, Air Toxics Committee.

6. *Peer-Review Process and Public Consultation:*

None.

7. *Status of Guideline:*

Not applicable.

8. *Key Risk Assessment Considerations:*

The State of New Jersey adopted the Northeast States for Coordinated Air Use Management's (Nescaum) risk-based chronic reference air level (RAL) of $165 \mu\text{g}/\text{m}^3$ as their RfC for xylenes (NJDEP, 1997b). The NESCAUM RALs were developed in order to assess the public health risks of occupational and non-occupational exposure to unleaded gasoline. Toxicological potencies of gasoline and the indicator compounds, including xylenes, were evaluated with respect to both cancer and non-cancer effects. In the assessment of non-cancer effects, critical effects were identified, and the most sensitive health effect associated with exposure to xylenes was considered to be reproductive and developmental toxicity. Upon identifying the most sensitive endpoint, studies were selected for a quantitative risk assessment based on an evaluation of study design and toxicological relevance. In evaluating the non-cancer threshold effects, uncertainty factors were applied in order to account for inter- and intraspecies variability, exposure durations, and sensitive populations.

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

The risk screening procedure used by the AQPP considers only inhalation exposure. Refined risk assessments conducted by permit applicants consider all likely exposure pathways. URFs must be used to calculate inhalation risks for carcinogens, while cancer potency factors are used to calculate risks from oral and dermal exposures. For non-carcinogens, reference concentrations (RfCs) must be used for inhalation exposure, and reference doses (RfDs) for oral and dermal exposures. The calculated doses from each route of exposure are summed to yield the total dose.

11. *Other Relevant Factors:*

None.

11.6 Agency-Specific Summary: New York State.

1. *Name of Chemical:* Xylenes (CAS# 1330-20-7)

2. *Agency:* New York State Department of Environmental Conservation (NYSDEC), Division of Air Resources.

3. *Guideline Value(s):*

The Short-term Guideline Concentration (SGC) for the sum of all three xylene isomers is 100,000 $\mu\text{g}/\text{m}^3$ (1-hour average) and the Annual Guideline Concentration (AGC) is 300 $\mu\text{g}/\text{m}^3$.

4. *Application:*

The NYSDEC guidelines for the control of toxic ambient air contaminants is intended primarily for use in the decision-making process of permitting emissions (6NYCRR Parts 200, 201, 212 and 257), and for application of certificates of operation for sources of air contamination. The regulatory process used in NYSDEC provides both short- and long-term guidelines to establish appropriate control requirements under existing statutes. The guidelines have been developed to aid the regulatory decision-making process using scientific data and professional judgement. However, they have not been subjected to the same degree of review as applied to an environmental standard.

5. *Documentation Available:*

NYSDEC, 1991. New York State Air Guide-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Division of Air Resources, Albany, New York.

Key Reference(s):

ACGIH, 1991. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices 1990-1991. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, Ohio.

US EPA, 1989a. Health Effects Assessment Summary Tables. United States Environmental Protection Agency, Office of Research and Development (ORD). Fourth Quarter, FY 1989. October 1989.

US EPA, 1989b. Integrated Risk Information System (IRIS) Computerized Database. United States Environmental Protection Agency, Washington, D.C.

6. *Peer-Review Process and Public Consultation:*

Peer-reviewed data and computer models were used in the development of the scientific documents

supporting the air guidelines. Scientific and professional judgment were employed in the toxicological assessment of contaminant classification and in the screening model analysis.

There are opportunities for public consultation, including the option to review the guidance used in the development of guidelines under certain circumstances and/or the option to develop an ambient air guideline for a contaminant not listed in the current guidelines.

7. Status of Guideline(s):

Current.

8. Key Risk Assessment Considerations:

Xylenes are classified as moderate toxicity air contaminants (Table III, Appendix C of NYSDEC, 1991). Moderate toxicity air contaminants are defined as animal oncogenes, developmental and reproductive toxicants, genotoxic chemicals and other chemicals posing a health hazard to humans.

The AGC was adopted from the US EPA's IRIS Reference Concentration (RfC) of 0.3 mg/m³ (300 µg/m³) for mixed xylenes (1989). The RfC for xylenes has been withdrawn pending review by that Agency's risk assessment work group. The SGC was derived from the ACGIH (1991) Threshold Limit Value-Time Weighted Average (TLV-TWA) by dividing the TLV-TWA (434 mg/m³) by 4.2 and rounding down to 100,000 µg/m³. The SGC was calculated as follows:

$$SGC = 434 \text{ mg/m}^3 / 4.2 = 103 \text{ mg/m}^3 \approx 100,000 \text{ µg/m}^3$$

The factor used above as the divisor is based on adjusting 8 hours/day, 5 days/week occupational exposure to 24 hours/day, 7 days/week environmental exposure (i.e., factor of 4.2).

9. Key Risk Management Considerations:

Specific computer models have been identified by the agency for use in impact screening as required in the permitting process.

10. Multimedia Considerations of Guidelines:

The NYSDEC guideline considers only human exposure to contaminants in air.

11. Other Relevant Factors:

The NYSDEC has recognized that the US EPA has withdrawn the RfC for xylenes. Nevertheless, NYSDEC has chosen to maintain the US EPA (1989) value of 300 µg/m³ as the AGC for xylenes until the US EPA posts a new RfC (NYSDEC, 1997).

11.7 Agency-Specific Summary: World Health Organization (WHO)

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* World Health Organization

3. *Guideline Value(s):*
None.

4. *Application:*
None.

5. *Documentation Available:*
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

6. *Peer-Review Process and Public Consultation:*
Not applicable.

7. *Status of Guideline:*
Not applicable.

8. *Key Risk Assessment Considerations:*
None.

9. *Key Risk Management Considerations:*
None.

10. *Multimedia Considerations of Guidelines:*
None.

11. *Other Relevant Factors:*
None.

11.8 Agency-Specific Summary: The Netherlands

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)
2. *Agency:* Netherlands Ministry of Housing, Spatial Planning and the Environment
3. *Guideline Value(s):*

Xylenes are classified as class 2 gaseous substances (gO.2). This classification imposes an emission standard of 100,000 $\mu\text{g}/\text{m}^3$ given a mass flow rate of 2.0 kg/hr or more. This standard is applied as a half-hourly average upper emission limit. (Netherlands Emission Regulations Staff Office, 1992). The Netherlands has also adopted a maximum immissible (sic) concentration (MIC) of 240 $\mu\text{g}/\text{m}^3$ for the sum of all three xylene isomers, applied as a three hour emission limit from the regional MIC developed by the province of Groningen. A target negligible concentration value has yet to be identified for xylenes.

4. *Application:*

These emission regulations are intended for use by all licensing authorities in the Netherlands in order to standardise the rules by which emissions are regulated in conjunction with licensing. These emission standards are to be applied as the maximum permissible emission concentration for different waste gas components on a facility specific basis. They are applied to emissions occurring at each source and at the point from which the waste gases leave the processing unit.

Compounds have been categorised into substance classes based on their respective toxicological profiles. There are four substance categories into which compounds are divided (carcinogens, particulates (general), organic or inorganic particulates, and organic or inorganic matter in gaseous or vaporous forms). The emission standard is based on a mass flow limit which has been established for each substance class derived from the application of best available technology. When the untreated mass flow rate of a substance or a class of substances exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting the compound or compounds in that class. Untreated mass flow is defined as "the mass of a particular single substance or summed masses of substances in the same class emitted per unit of time and before any treatment by means of add-on technology" (Netherlands Emission Regulations Staff Office, 1992).

The environmental quality objectives present effects oriented risk levels which have been established for use in a progressive criteria setting program in the Netherlands. The objective of this program is to reduce the emissions of priority substances to a concentration at which the occurrence of adverse effects are considered to be negligible. This program details a long term environmental quality objective which establishes a target value for which emissions of priority substances must be maintained below. This target value is either set at the naturally occurring background level, or a negligible effects concentration which has been established for that compound based on the available toxicological

literature. This progressive approach will require facility specific emissions to be kept below a limit or a guidance value which will eventually be tightened to reach the goal of the target value for the compound in question. These guidance or limit values are either air quality statutory requirements or non statutory regional specific MIC levels.

5. Documentation Available:

Netherlands Emission Regulations Staff Office, 1992. Netherlands Emission Regulations - Air (NeR). Netherlands Emission Regulations Staff Office. Bilthoven, The Netherlands.

Netherlands Ministry of Housing, Spatial Planning and the Environment, 1994. Environmental Quality Objectives in the Netherlands - A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment. The Hague, The Netherlands.

6. Peer-review Process and Public Consultation:

The Netherlands Emission Regulations and the Environmental Quality Objectives documents were not peer-reviewed or released for public comment.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

The mass flow limits for the substance classes are based on the German TA-luft Program (Directorate-General for Environmental Protection, 1997). When the untreated mass flow per class exceeds the critical mass flow limit established for that class, the standard in question is applied to the total discharge for all sources emitting compounds in that class. The standard serves as an average half-hourly upper emission limit of 100,000 $\mu\text{g}/\text{m}^3$ in the case of a mass flow of 2.0 kg/hr or more upon the application of best available technology. Mass flow is defined as "the mass of a particular substance or group of substances from the same class emitted per unit of time" (Netherlands Emission Regulations Staff Office, 1992).

The regional MIC values applied in the environmental quality objectives program were derived by the Province of Groningen using the occupational hygiene based national 1982-1983 MAC's adjusted by a modifying factor. A modifying factor of 1,000 is applied for compounds classified by the International Agency for Research on Cancer (IARC) as a substance which may have carcinogenic properties, or for compounds which have been shown to cause reproductive or developmental effects. A factor of 150 was applied for all other substances. The MAC's from which the MIC's are derived are occupationally based exposure limits and these uncertainty factors account for the extrapolation from a 40 hour work week to a continuous 24 hour exposure level, and to adjust for exposure to the general

population (children, adults and elderly).

9. Key Risk Management Considerations:

These Netherlands Emission Regulations standards do not replace existent binding emission or national air quality legal regulations and/or standards. These standards are only to be used as a guidance for licensing agencies until the Dutch Emission Guidelines for the granting of licences is released under the *Environmental Protection Act*.

10. Multimedia Considerations of Guidelines:

None.

11. Other Relevant Factors:

None.

11.9 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. *Name of Chemical:* Xylenes (CAS# 1330-27-7)

2. *Agency:* Swedish Institute of Environmental Medicine

3. *Guideline Value(s):*

No guideline is available for xylenes. However, a long-term average of 10-100 ppb (approximately 40-400 $\mu\text{g}/\text{m}^3$) for the sum of toluene and the three xylene isomers has been suggested by Sweden's Institute of Environmental Medicine (1997).

4. *Application:*

Air emissions in Sweden are regulated by one of two authorities: i) the regional County Government Boards; or ii) the central authority called the National Licensing Board for Environmental Protection. The guidelines are generally applied to permitting of emissions from industrial, heat and power plants.

5. *Documentation Available:*

Institute of Environmental Medicine, 1997. Personal Communication: Ms. K. Victorin, Institute of Environmental Medicine, February 20, 1997.

Victorin, K., 1993. Health effects of urban air pollutants. Guideline values and conditions in Sweden. *Chemosphere* 27(9) 1691-1706.

6. *Peer-Review Process and Public Consultation:*

No Information available.

7. *Status of Guideline:*

Not information available.

8. *Key Risk Assessment Considerations:*

The Institute of Environmental Medicine has performed a number of health risk evaluations on chemicals found in combustion emissions. In general, the Institute develops air guideline values by taking the lowest-observed-effect-level in humans for that compound and applying a factor of between 100 and 1000. For cancer-causing chemicals, air guidelines may be based on a lifetime cancer risk of 1×10^{-5} .

A health risk assessment has been carried out for xylenes.

9. *Key Risk Management Considerations:*

No information available.

10. *Multimedia Considerations of Guidelines:*

No information available.

11. *Other Relevant Factors:*

A detailed review of the basis for the health risk assessment for xylenes was not carried out since the criteria documents for air quality were only available in Swedish (Institute of Environmental Medicine, 1997).

11.10 Agency-Specific Summary: Federal Government of Canada (CEPA)

1. *Name of Chemical:* Xylenes (CAS # 1330-20-7)

2. *Agency:* Environment Canada and Health Canada - *Canadian Environmental Protection Act*

3. *Guideline Value(s):*

Xylenes were assessed under the first Priority Substance List (PSL1). No specific air quality guideline value exists, however a provisional Tolerable Concentration (TC) of 180 µg/m³ has been identified for xylenes.

4. *Application:*

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and Health to prepare and publish a Priority Substances List (PSL) that identifies substances that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in Section 11 of the Act. The assessment of whether substances are toxic is based on the determination of whether they enter or are likely to enter the Canadian environment in an amount that could lead to exposure of humans or other biota at levels that could cause adverse effects.

Substances that are assessed as "toxic" may be placed on Schedule I of the Act and considered for possible development of regulations or guidelines.

5. *Documentation Available:*

Environment Canada and Health Canada, 1993a. *Canadian Environmental Protection Act* Priority Substances List Supporting Document: Xylenes - *Unedited Document*.

Environment Canada and Health Canada, 1993b. *Canadian Environmental Protection Act* Priority Substances List Assessment Report - Xylenes. Minister of Supply and Services Canada; Ottawa, Canada.

Environment Canada, PSL2 Secretariat, 1995. Report of the Ministers' Expert Advisory Panel on the Second Priority Substances List Under the *Canadian Environmental Protection Act* (CEPA). October, 1995.

Health Canada, 1996a. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Minister of Supply and Services Canada, Ottawa, Ontario.

Health Canada, 1996b. Canadian Environmental Protection Act-Priority Substances List Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances.

Key References:

Ungvary, G., and E. Tatrai, 1985. On the embryotoxic effects of benzene and its alkyl derivatives in mice, rats and rabbits. *Arch. Toxicol. Suppl.* 8, 425-430.

6. Peer-review Process and Public Consultation:

CEPA underwent comprehensive public consultation and review. PSL documents are based on peer-reviewed literature and are peer-reviewed prior to being released.

7. Status of Guideline:

Current.

8. Key Risk Assessment Considerations:

Although no specific air quality guideline has been set for xylenes by the Canadian Federal Government, a provisional Tolerable Concentration (TC) have been identified. The TC is defined as the airborne concentrations to which a person can be exposed continuously over a lifetime without deleterious effect (Health Canada, 1996a). A provisional TC has been derived for xylenes based the results of a rat developmental toxicity study. Environment Canada and Health Canada termed the study "limited" because the documentation of the protocol and results in the published account was incomplete (Environment Canada and Health Canada, 1993b). Maternal (unspecified) and fetal (skeletal retardation) toxicity were observed in rats exposed on days 7-15 of gestation to xylenes at 250 mg/m³ (the lowest administered concentration). The TC was calculated using this lowest-observed-effects-level (LOEL) adjusted by:

1. a factor of 1,000 (10x to account for interspecies extrapolation (rats to humans), 10x to account for intraspecies variation, and 10x for extrapolating from a LOEL to a no-observed-effects-level and the "limitations" of the critical study);
2. the ratio of the inhalation volume/body weight of rats [(0.11 m³/day)/0.35 kg] to humans aged 5 to 11 years [(12 m³/day)/27 kg].

These adjustments resulted in a provisional TC of 0.18 mg/m³. The limitations of the critical study are not explicitly identified in the Supporting Documentation, however other reviews have noted that the documentation was insufficient to assess experiential protocol and maternal toxicity and that results were reported as the number of fetuses rather than litters (IARC, vol 47).

9. *Key Risk Management Considerations:*

Not applicable.

10. *Multimedia Considerations of Guidelines:*

Not applicable.

11. *Other Relevant Factors:*

Not applicable.

12.0 Acronyms, Abbreviations and Definitions

AAL	<i>Allowable Ambient Level</i> (Massachusetts)
AAQC	<i>Ambient Air Quality Criteria</i> - used by the Ontario Ministry of the Environment to define the potential for causing an adverse effect
ACGIH	<i>American Conference of Governmental Industrial Hygienists</i> - a non-governmental organization which establishes occupational safety exposure limits for workers
AGC	<i>Annual guideline Concentration</i> (New York State)
ATSDR	<i>Agency for Toxic Substances and Disease Registry</i> - an agency of the US Department of Health & Human Services
CAPCOA	<i>California Air Pollution Control Officers Association</i>
CAS	<i>Chemical Abstracts Service</i> - ascribes a unique, identification (registry) number to each chemical to help clarify multiple listings for the same chemical structure
CEPA	<i>Canadian Environmental Protection Act</i>
GLC	<i>Ground Level Concentration</i> - the concentration of contaminant predicted by dispersion modelling
HEAST	<i>Health Effects Assessment Summary Tables</i> - prepared by US EPA's Office of Health and Environmental Assessment. HEAST contains risk assessment information on chemicals that have undergone reviews, although generally not as extensive as the reviews conducted under IRIS
HEC	<i>Human Equivalent Concentration</i>
IARC	<i>International Agency for Research on Cancer</i>
IRIS	<i>Integrated Risk Information System</i> - a database published by the US EPA containing risk assessment information on a wide range of chemicals
IRSL	<i>Initial Risk Screening Level</i> - a limit corresponding to a one in a million lifetime risk of cancer used by Michigan for screening new sources of emissions
ITSL	<i>Interim Threshold Screening Level</i> - similar to the IRSL, however, derived from the RfC for non-carcinogens
LC₅₀	The concentration of a substance in the medium (eg., air, water, soil) to which a test species is exposed, that will kill 50% of the population of that given species
LD₅₀	The dose of a substance given to a test species, that will kill 50% of the population of that given species
LOAEL	<i>Lowest-Observed-Adverse-Effect Level</i>
LOEL	<i>Lowest-Observed-Effect Level</i>
MAC	<i>Maximum Acceptable Concentration</i>
MACT	<i>Maximum Achievable Control Technology</i>
μg	a microgram, one millionth of a gram
mg	a milligram, one thousandth of a gram
MRL	<i>Minimal Risk Level</i> - a term used by ATSDR, which defines a daily exposure [either

	from an inhalation or oral route] not likely to induce adverse non-carcinogenic effects within a given time period, ie., acute, intermediate, or chronic
MOE	<i>Ontario Ministry of the Environment</i> ; between 1993 and 1997 known as MOEE or <i>Ontario Ministry of Environment and Energy</i>
ng	a nanogram, one billionth of a gram
NIEHS	<i>National Institute of Environmental Health Sciences (USA)</i>
NIOSH	<i>National Institute for Occupational Safety and Health</i> (an agency of the US Department of Health & Human Services)
NOAEL	<i>No-Observed-Adverse-Effect Level</i>
NOEL	<i>No-Observed-Effect Level</i>
NPRI	<i>National Pollutant Release Inventory</i>
NTP	<i>National Toxicology Program (USA)</i>
OEHHA	<i>Office of Environmental Health Hazard Assessment (California EPA)</i>
OEL	<i>Occupational Exposure Level</i>
OSHA	<i>Occupational Safety and Health Administration</i> - a branch of the US Dept of Labour
PEL	<i>Permissible Exposure Limit</i> (OSHA air standard)
POI	<i>Point of Impingement</i> - used in conjunction with dispersion modelling to define the area in which the maximum ground level concentration (GLC) of a contaminant is predicted to occur
ppb	parts per billion
ppm	parts per million
REL	<i>Either 'Reference Exposure Level' as used by the California EPA which defines the concentration at or below which no adverse health effects are expected in the general population or 'Recommended Exposure Limit' used by both NIOSH and ATSDR</i>
RfC	<i>Reference Concentration</i> - an estimate of a daily inhalation exposure not likely to induce deleterious non-cancer health effects during a lifetime
RfD	<i>Reference Dose</i> - an estimate of a daily exposure dose not likely to induce adverse health effects during a lifetime
RTECS	<i>Registry of Toxic Effects of Chemical Substances</i> - database maintained by NIOSH
SGC	<i>Short-term Guideline Concentration</i> (New York State)
STEL	<i>Short-term Exposure Limit</i>
TC	<i>Tolerable Concentration</i> - used by Health Canada to define the airborne concentration to which a person can be exposed for a lifetime without deleterious effects (for non-carcinogens)
TC₀₅	<i>Tumourigenic concentration</i> - the concentration of a contaminant in air generally associated with a 5% increase in incidence or mortality due to tumours
TD₀₅	<i>Tumourigenic dose</i> - the total intake of a contaminant generally associated with a 5% increase in incidence or mortality due to tumours

TLV	<i>Threshold Limit Value</i> - an exposure concentration that should not induce an adverse effect in a work environment
TWA	<i>Time-Weighted-Average</i> - allowable exposure averaged over an 8-hour workday or 40-hour work week
US EPA	<i>United States Environmental Protection Agency</i>
WHO	<i>World Health Organization</i>